

Set	Items	Description
?	E AU=RHEE,	J?

Ref	Items	Index-term
E1	26	AU=RHEE, J- S
E2	2	AU=RHEE, J- Y
E3	0	*AU=RHEE, J?
E4	2	AU=RHEE, JA
E5	2	AU=RHEE, JAE CHI N
E6	1	AU=RHEE, JAE HAN
E7	2	AU=RHEE, JAE HO
E8	4	AU=RHEE, JAE HUI
E9	1	AU=RHEE, JAE JI N
E10	4	AU=RHEE, JAE K.
E11	37	AU=RHEE, JAE KEOL
E12	6	AU=RHEE, JAE KU

Enter P or PAGE for more  
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Ref	Items	Index-term
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E2	1	AU=RHEE, JCON- SHI K
E3	0	*AU=RHEE, JCON?
E4	1	AU=RHEE, JCONG E.
E5	1	AU=RHEE, JCONG EUI
E6	1	AU=RHEE, JCONG GEUN
E7	1	AU=RHEE, JCONG HYUK
E8	2	AU=RHEE, JCONG EUI
E9	10	AU=RHEE, JCONG GEUN
E10	6	AU=RHEE, JCONG SUP
E11	2	AU=RHEE, JCONG YONG
E12	2	AU=RHEE, JCONKYU

Enter P or PAGE for more  
? E AU=RHEE, JCON- HAENG

Ref	Items	Index-term
E1	8	AU=RHEE, JCON WHAN
E2	2	AU=RHEE, JCON WON
E3	27	*AU=RHEE, JCON- HAENG
E4	1	AU=RHEE, JCON- SEONG
E5	25	AU=RHEE, JCON- SHI CK
E6	1	AU=RHEE, JCON- SHI K
E7	1	AU=RHEE, JCONG E.
E8	1	AU=RHEE, JCONG EUI
E9	1	AU=RHEE, JCONG GEUN
E10	1	AU=RHEE, JCONG HYUK
E11	2	AU=RHEE, JCONG EUI
E12	10	AU=RHEE, JCONG GEUN

Enter P or PAGE for more  
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S1 27 AU= RHEE, JCON- HAENG  
? RD

>>>Duplicate detection is not supported for File 393.

>>>Duplicate detection is not supported for File 391.

>>>Records from unsupported files will be retained in the RD set.  
Page 1

S2 15 RD (unique items)  
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 25810 FLAGELLIN  
 S3 0 S2 AND FLAGELLIN  
 ? S S2 AND FLAG?  
 15 S2  
 369460 FLAG?  
 S4 0 S2 AND FLAG?  
 ? S S2  
 S5 15 S2  
 ? T S5/3, K/1-5  
 >>>KW C option is not available in file(s): 399

5/3, K/1 (Item 1 from file: 24)  
 DI ALCOG R) File 24: CSA Life Sciences Abstracts  
 (c) 2009 CSA. All rts. reserv.

0003663529 IP ACCESSI ON NO: 9163829  
 The dysfunction and abnormal signaling pathway of dendritic cells loaded by  
 tumor antigen can be overcome by neutralizing VEGF in multiple myeloma

Yang, Deok-Hwan; Park, Jung-Sun; Jin, Chun-Ji; Kang, Hyun-Kyu; Nam  
 Jong-Hee; Rhee, Joon-Haeng; Kim Yeo-Kyeong; Chung, Sang-Young;  
 Choi, So-Jin-Na; Kim Hyeoung-Joon; Chung, Ik-Joo; Lee, Je-Jung  
 Department of Hematology-Oncology, Chonnam National University Hwasun  
 Hospital, Hwasun, Jeonnam, South Korea, [mailto:drjejung@chonnam.ac.kr]

Leukemia Research, v 33, n 5, p 665-670, May 2009  
 PUBLICATION DATE: 2009

PUBLISHER: Elsevier Science, P. O. Box 800 Kidlington Oxford OX5 1DX UK,  
 [mailto:nlinfo-f@elsevier.nl], [URL: http://www.elsevier.nl]

DOCUMENT TYPE: Journal Article  
 RECORD TYPE: Abstract  
 LANGUAGE: English  
 SUMMARY LANGUAGE: English  
 ISSN: 0145-2126  
 FILE SEGMENT: Immunology Abstracts

Yang, Deok-Hwan; Park, Jung-Sun; Jin, Chun-Ji; Kang, Hyun-Kyu; Nam  
 Jong-Hee; Rhee, Joon-Haeng; Kim Yeo-Kyeong; Chung, Sang-Young;  
 Choi, So-Jin-Na; Kim Hyeoung-Joon...

5/3, K/2 (Item 2 from file: 24)  
 DI ALCOG R) File 24: CSA Life Sciences Abstracts  
 (c) 2009 CSA. All rts. reserv.

0003522208 IP ACCESSI ON NO: 7041018  
 Vibrio vulnificus Vulnibactin, But Not Metalloprotease VvpE, Is Essentially  
 Required for Iron-Uptake from Human Holotransferrin

Kim Choon-Mee; Park, Ra-Young; Park, Jeong-Hee; Sun, Hui-Yu; Bai,  
 Young-Hoon; Ryu, Phil-Yeol; Kim Soo-Young; Rhee, Joon-Haeng;  
 Shin, Sung-Heul  
 Research Center for Resistant Cells, Chosun University Medical School;  
 Gwangju 501-759, South Korea, [mailto:shsin@chosun.ac.kr]

Biological & Pharmaceutical Bulletin, v 29, n 5, p 911-918, May 2006  
 PUBLICATION DATE: 2006

DOCUMENT TYPE: Journal Article

RECORD TYPE: Abstract

LANGUAGE: English

SUMMARY LANGUAGE: English

ISSN: 0918-6158

ASFA NO: CS0728831

FILE SEGMENT: Bacteriology Abstracts (Microbiology B)

... Park, Jeong-Hee; Sun, Hui-Yu; Bai, Young-Hoon; Ryu, Phil-Yeol; Kim Soo-Young; Rhee, Joon-Haeng; Shin, Sung-Heui

5/3, K/3 (Item 3 from file: 24)

DI ALOG R) File 24: CSA Life Sciences Abstracts

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0003520430 IP ACCESSI ON NO: 6434094

Inactivation of *Vibrio vulnificus* Hemolysin by Oligomerization but Not Proteolysis

Shin, Sung-Heui; Sun, Hui-Yu; Choi, M-Hwa; Park, Ra-Young; Bai, Young-Hoon; Kim Choon-Mee; Kim Soo-Young; Kim Young-Ran; Lee, Shee-Eun; Rhee, Joon-Haeng  
Research Center for Resistant Cells, Chosun University Medical School

Biological & Pharmaceutical Bulletin, v 28, n 7, 2005

PUBLICATION DATE: 2005

PUBLISHER: Pharmaceutical Society of Japan, 2-12-15, Shibuya Shibuya-ku  
Tokyo 150-0002 Japan, [mailto:ronb@pharm.or.jp],  
[URL: http://bpb.pharm.or.jp]

DOCUMENT TYPE: Journal Article

RECORD TYPE: Abstract

LANGUAGE: English

SUMMARY LANGUAGE: English

ISSN: 0918-6158

FILE SEGMENT: Bacteriology Abstracts (Microbiology B)

... Bai, Young-Hoon; Kim Choon-Mee; Kim Soo-Young; Kim Young-Ran;  
Lee, Shee-Eun; Rhee, Joon-Haeng

5/3, K/4 (Item 4 from file: 24)

DI ALOG R) File 24: CSA Life Sciences Abstracts

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0003158407 IP ACCESSI ON NO: 7899305

*Vibrio vulnificus* metalloprotease VvpE is essentially required for swarming

Kim Choon-Mee; Park, Ra-Young; Chun, Ho-Jong; Kim Soo-Young; Rhee, Joon-Haeng; Shin, Sung-Heui  
Research Center for Resistant Cells, Chosun University Medical School,  
Gwangju, Korea, [mailto:shsin@chosun.ac.kr]

FEMS Microbiology Letters, v 269, n 1, p 170-179, April 2007

PUBLICATION DATE: 2007

PUBLISHER: Elsevier Science, P.O. Box 211

DOCUMENT TYPE: Journal Article

RECORD TYPE: Abstract

LANGUAGE: English

SUMMARY LANGUAGE: English

ISSN: 0378-1097

FILE SEGMENT: Bacteriology Abstracts (Microbiology B)

Kim Choon-Mee; Park, Pa-Young; Chun, Ho-Jong; Kim Soo-Young; Rhee, Joon-Haeng; Shin, Sung-Heui

5/3, K/5 (Item 1 from file: 393)  
 DIALCOG File 393: Beilstein Database - Abstracts  
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Beilstein Abstract Id: 6553384

Title: *Vibrio vulnificus* Vulnibactin, But Not Metalloprotease VvpE, Is Essentially Required for Iron Uptake from Human Holotransferrin

Document Type: Journal Record Type: Abstract

Author: Kim Choon-Mee; Park, Pa-Young; Park, Jeong-Hee; Sun, Hui-Yu; Bai, Young-Hoon; Ryu, Phil-Yeol; Kim Soo-Young; Rhee, Joon-Haeng; Shin, Sung-Heui

Citation: Biol. Pharm. Bull. (2006) Series: 29-5, 911 - 918 CODEN: BPBLEO Language: English

Abstract Language: English

... Author: Park, Jeong-Hee; Sun, Hui-Yu; Bai, Young-Hoon; Ryu, Phil-Yeol; Kim Soo-Young; Rhee, Joon-Haeng; Shin, Sung-Heui

? DS

Set	Items	Description
S1	27	ALL RHEE, JOON-HAENG
S2	15	RD (unique items)
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S4	0	S2 AND FLAG?
S5	15	S2

? T S5/3, K/6-15

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5/3, K/6 (Item 2 from file: 393)  
 DIALCOG File 393: Beilstein Database - Abstracts  
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Beilstein Abstract Id: 6505604

Title: Inactivation of *Vibrio vulnificus* hemolysin by oligomerization but not proteolysis

Document Type: Journal Record Type: Abstract

Author: Shin, Sung-Heui; Sun, Hui-Yu; Choi, M-Hwa; Park, Pa-Young; Bai, Young-Hoon; Kim Choon-Mee; Kim Soo-Young; Kim Young-Ran; Lee, Shee-Eun; Rhee, Joon-Haeng

Citation: Biol. Pharm. Bull. (2005) Series: 28-7, 1294 - 1297 CODEN: BPBLEO Language: English

Abstract Language: English

... Author: Bai, Young-Hoon; Kim Choon-Mee; Kim Soo-Young; Kim Young-Ran; Lee, Shee-Eun; Rhee, Joon-Haeng

5/3, K/7 (Item 1 from file: 399)  
 DIALCOG File 399: CA SEARCH(R)  
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148260207 CA: 148(12)260207u JOURNAL  
 Induction of multiple myeloma-specific cytotoxic T lymphocyte stimulation by dendritic cell pulsing with purified and optimized myeloma cell lysates

FLAGELLIN0585880.txt

AUTHOR(S): Lee, Je-Jung; Choi, Bo-Hwa; Kang, Hyun-Kyu; Park, Myong-Suk; Park, Jung-Sun; Kim Sang-Ki; Pham Thanh-Nhan Nguyen; Cho, Duck; Nam Jong-Hee; Kim Young-Jin; Rhee, Joon-Haeng; Yang, Deok-Hwan; Kim Yeo-Kyeoung; Kim Hyeoung-Joon; Chung, Ik-Joo

LOCATION: Clinical Vaccine R&D Center, Chonnam National University  
Department of Hematology - Oncology, Chonnam National University Hwasun Hospital, Jeonnam, S. Korea

JOURNAL: Leuk. Lymphoma (Leukemia & Lymphoma) DATE: 2007 VOLUME: 48  
NUMBER: 10 PAGES: 2022-2031 CODEN: LELYEA ISSN: 1042-8194 LANGUAGE: English PUBLISHER: Informa Healthcare

5/3, K/8 (Item 2 from file: 399)

DIALOG(R) File 399: CA SEARCH(R)

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146498196 CA: 146(25)498196y JOURNAL

Down-regulation of cellular vascular endothelial growth factor levels induces differentiation of leukemic cells to functional leukemic-dendritic cells in acute myeloid leukemia

AUTHOR(S): Kang, Hyun-Kyu; Park, Jung-Sun; Kim Sang-Ki; Choi, Bo-Hwa; Pham Thanh-Nhan Nguyen; Zhu, Xiao-Wei; Cho, Duck; Nam Jong-Hee; Kim Young-Jin; Rhee, Joon-Haeng; Chung, Ik-Joo; Kim Hyeoung-Joon; Lee, Je-Jung

LOCATION: Department of Hematology-Oncology, Chonnam National University Medical School, Gwangju, S. Korea

JOURNAL: Leuk. Lymphoma (Leukemia & Lymphoma) DATE: 2006 VOLUME: 47  
NUMBER: 10 PAGES: 2224-2233 CODEN: LELYEA ISSN: 1042-8194 LANGUAGE: English PUBLISHER: Informa Healthcare

5/3, K/9 (Item 3 from file: 399)

DIALOG(R) File 399: CA SEARCH(R)

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146224476 CA: 146(12)224476f JOURNAL

X-gal inhibits the swarming of *Vibrio* species

AUTHOR(S): Kim Moon-Young; Park, Ra-Young; Bai, Young-Hoon; Chung, Yoon-Young; Kim Choon-Mee; Kim Soo-Young; Rhee, Joon-Haeng; Shin, Sung-Heui

LOCATION: Research Center for Resistant Cells, Chosun University Medical School, Gwangju, 501-759, S. Korea

JOURNAL: J. Microbiol. Methods (Journal of Microbiological Methods)  
DATE: 2006 VOLUME: 66 NUMBER: 3 PAGES: 552-555 CODEN: JMDQ ISSN: 0167-7012 PUBLISHER: Elsevier B.V.  
0167-7012 CODEN: JMDQ ISSN: 0167-7012(06)00018-2 LANGUAGE: English PUBLISHER: Elsevier B.V.

5/3, K/10 (Item 4 from file: 399)

DIALOG(R) File 399: CA SEARCH(R)

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146077702 CA: 146(5)77702w JOURNAL

Swarming differentiation of *Vibrio vulnificus* downregulates the expression of the *vvhBA* hemolysin gene via the LuxS quorum-sensing system

AUTHOR(S): Kim Moon-Young; Park, Ra-Young; Choi, M-Hwa; Sun, Hui-Yu; Kim Choon-Mee; Kim Soo-Young; Rhee, Joon-Haeng; Shin, Sung-Heui

LOCATION: Research Center for Resistant Cells, Chosun University Medical School, Gwangju, 501-759, S. Korea

JOURNAL: J. Microbiol. (Seoul, Repub. Korea) (Journal of Microbiology (Seoul, Republic of Korea)) DATE: 2006 VOLUME: 44 NUMBER: 2 PAGES: 226-232 CODEN: JOMFG ISSN: 1225-8873 LANGUAGE: English PUBLISHER: Microbiological Society of Korea

5/3, K/11 (Item 5 from file: 399)  
 DIALOG(R) File 399: CA SEARCH(R)  
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145203874 CA: 145(11)203874y JOURNAL  
 Effect of the crp mutation on the utilization of transferrin-bound iron  
 by *Vibrio vulnificus*  
 AUTHOR(S): Choi, M-Hwa; Sun, Hui-Yu; Park, Ra-Young; Kim Choon-Mee;  
 Bai, Young-Hoon; Kim Young-Ran; Rhee, Joon-Haeng; Shin, Sung-Heui  
 LOCATION: Research Center for Resistant Cells, Chosun University Medical  
 School, Gwangju, S. Korea  
 JOURNAL: FEMS Microbiol. Lett. (FEMS Microbiology Letters) DATE: 2006  
 VOLUME: 257 NUMBER: 2 PAGES: 285-292 CODEN: FMLED7 ISSN: 0378-1097  
 LANGUAGE: English PUBLISHER: Blackwell Publishing Ltd.

5/3, K/12 (Item 6 from file: 399)  
 DIALOG(R) File 399: CA SEARCH(R)  
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145060561 CA: 145(4)60561f JOURNAL  
 Suppression and inactivation of *Vibrio vulnificus* hemolysin in cirrhotic  
 ascites, a human ex vivo experimental system  
 AUTHOR(S): Choi, M-Hwa; Park, Ra-Young; Sun, Hui-Yu; Kim Choon-Mee;  
 Bai, Young-Hoon; Lee, Shee-Eun; Kim Soo-Young; Kim Young-Ran; Rhee,  
 Joon-Haeng; Shin, Sung-Heui  
 LOCATION: Research Center for Resistant cells, Chosun University Medical  
 School, Gwangju, S. Korea  
 JOURNAL: FEMS Immunol. Med. Microbiol. (FEMS Immunology and Medical  
 Microbiology) DATE: 2006 VOLUME: 47 NUMBER: 2 PAGES: 226-232 CODEN:  
 FIMEV ISSN: 0928-8244 LANGUAGE: English PUBLISHER: Blackwell Publishing  
 Ltd.

5/3, K/13 (Item 7 from file: 399)  
 DIALOG(R) File 399: CA SEARCH(R)  
 (c) 2009 American Chemical Society. All rts. reserv.

143244771 CA: 143(14)244771q JOURNAL  
*Vibrio vulnificus* metalloprotease VvpE has no direct effect on the  
 iron assimilation from human holotransferrin  
 AUTHOR(S): Shin, Sung-Heui; Sun, Hui-Yu; Park, Ra-Young; Kim Choon-Mee;  
 Kim Soo-Young; Rhee, Joon-Haeng  
 LOCATION: Research Center for Resistant Cells, Department of Microbiology  
 , Chosun University Medical School, Gwangju, 501-759, S. Korea  
 JOURNAL: FEMS Microbiol. Lett. (FEMS Microbiology Letters) DATE: 2005  
 VOLUME: 247 NUMBER: 2 PAGES: 221-229 CODEN: FMLED7 ISSN: 0378-1097  
 PUBLISHER ITEM IDENTIFIER: 0378-1097(05)00297-1 LANGUAGE: English  
 PUBLISHER: Elsevier B.V.

5/3, K/14 (Item 8 from file: 399)  
 DIALOG(R) File 399: CA SEARCH(R)  
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138283805 CA: 138(19)283805v JOURNAL  
 Effect of salinity, temperature, and glucose on the production of *Vibrio*  
*vulnificus* hemolysin  
 AUTHOR(S): Kim Hyun-Soo; Shin, Sung-Heui; Park, Hae-Ryoung; Lee,  
 Shee-Eun; Kim Choon-Mee; Kim Soo-Young; Kim Young-Ran; Lee, Hyun-Chul;  
 Chung, Sun-Sik; Rhee, Joon-Haeng  
 LOCATION: Department of Microbiology, Chonnam National University Medical  
 Page 6

FLAGELLI N10585880.txt

School, Kwangju, 501-746, S. Korea

JOURNAL: J. Bacteriol. Virol. (Journal of Bacteriology and Virology)

DATE: 2002 VOLUME: 32 NUMBER: 4 PAGES: 355-365 CODEN: JBVOAH ISSN: 1598-2467 LANGUAGE: English PUBLISHER: Journal of Bacteriology and Virology

5/3, K/15 (Item 9 from file: 399)

DIALOG(R) File 399: CA SEARCH(R)

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123006941 CA: 123(1) 6941n JOURNAL

A study on the pathogenetic activity of the protease and hemolysin produced by *Vibrio vulnificus*. I. Biological properties of the hemolysin produced by *Vibrio vulnificus*

AUTHOR(S): Rhee, Joon-Haeng; Lee, Shee-Eun; Kwon, Hyoung-Cheol; Chang, Heung-Shik; Ryu, Phil-Youl; Chung, Sun-Sik

LOCATION: Medical School, Chonnam National University, Kwangju, 501-190, S. Korea

JOURNAL: Taehan Msaengmul Hakhoechi DATE: 1994 VOLUME: 29 NUMBER: 5

PAGES: 381-98 CODEN: TMHCDX ISSN: 0253-3162 LANGUAGE: Korean

? E AU=LEE, SHEE-EUN

Ref	Items	Index-term
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E3	3	AU=LEE, SHEE-YONG
E4	1	AU=LEE, SHEEN WOO
E5	2	AU=LEE, SHEEN-JE
E6	1	AU=LEE, SHEEN-MOK
E7	11	AU=LEE, SHEEN-WOO
E8	11	AU=LEE, SHEENA
E9	1	AU=LEE, SHEENA R
E10	2	AU=LEE, SHEENA R
E11	13	AU=LEE, SHEEYONG
E12	4	AU=LEE, SHEE-VEN

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S6 9 AU=LEE, SHEE-EUN

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>>>Duplicate detection is not supported for File 393.

>>>Duplicate detection is not supported for File 391.

>>>Records from unsupported files will be retained in the RD set.

S7 5 RD (unique items)

? T S7/3, K/1-5

>>>KWC option is not available in file(s): 399

7/3, K/1 (Item 1 from file: 24)

DIALOG(R) File 24: CSA Life Sciences Abstracts

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0003520430 I P ACCESSION NO: 6434094

Inactivation of *Vibrio vulnificus* Hemolysin by Oligomerization but Not Proteolysis

Shin, Sung-Heui; Sun, Hui-Yu; Choi, M-Hwa; Park, Ra-Young; Bai, Young-Hoon; Kim, Choon-Mee; Kim, Soo-Young; Kim, Young-Ran; Lee, Shee-Eun; Rhee, Joon-Haeng  
Research Center for Resistant Cells, Chosun University Medical School

Biological & Pharmaceutical Bulletin, v 28, n 7, 2005  
PUBLICATION DATE: 2005

PUBLISHER: Pharmaceutical Society of Japan, 2-12-15, Shibuya Shibuya-ku  
Tokyo 150-0002 Japan, [mailto:ronb@pharm.or.jp],  
[URL: http://bbp.pharm.or.jp]

DOCUMENT TYPE: Journal Article  
RECORD TYPE: Abstract  
LANGUAGE: English  
SUMMARY LANGUAGE: English  
ISSN: 0918-6158  
FILE SEGMENT: Bacteriology Abstracts (Microbiology B)

...Park, Ra-Young; Bai, Young-Hoon; Kim Choon-Mee; Kim Soo-Young;  
Kim Young-Ran; Lee, Shee-Eun; Rhee, Joon-Haeng

7/3, K/2 (Item 1 from file: 393)  
DIALOG(R) File 393: Beilstein Database - Abstracts  
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Beilstein Abstract Id: 6505604  
Title: Inactivation of *Vibrio vulnificus* hemolysin by oligomerization but  
not proteolysis  
Document Type: Journal Record Type: Abstract  
Author: Shin, Sung-Heui; Sun, Hui-Yu; Choi, M-Hwa; Park, Ra-Young;  
Bai, Young-Hoon; Kim Choon-Mee; Kim Soo-Young; Kim Young-Ran  
; Lee, Shee-Eun; Rhee, Joon-Haeng  
Citation: Biol. Pharm. Bull. (2005) Series: 28-7, 1294 - 1297 CODEN:  
BPBLEO Language: English  
Abstract Language: English

... Author: Park, Ra-Young; Bai, Young-Hoon; Kim Choon-Mee; Kim  
Soo-Young; Kim Young-Ran; Lee, Shee-Eun; Rhee,  
Joon-Haeng

7/3, K/3 (Item 1 from file: 399)  
DIALOG(R) File 399: CA SEARCH(R)  
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145060561 CA: 145(4) 60561f JOURNAL  
Suppression and inactivation of *Vibrio vulnificus* hemolysin in cirrhotic  
ascites, a human ex vivo experimental system  
AUTHOR(S): Choi, M-Hwa; Park, Ra-Young; Sun, Hui-Yu; Kim Choon-Mee;  
Bai, Young-Hoon; Lee, Shee-Eun; Kim Soo-Young; Kim Young-Ran; Rhee,  
Joon-Haeng; Shin, Sung-Heui  
LOCATION: Research Center for Resistant cells, Chosun University Medical  
School, Gwangju, S. Korea  
JOURNAL: FEMS Immunol. Med. Microbiol. (FEMS Immunology and Medical  
Microbiology) DATE: 2006 VOLUME: 47 NUMBER: 2 PAGES: 226-232 CODEN:  
FIM EV ISSN: 0928-8244 LANGUAGE: English PUBLISHER: Blackwell Publishing  
Ltd.

7/3, K/4 (Item 2 from file: 399)  
DIALOG(R) File 399: CA SEARCH(R)  
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138283805 CA: 138(19) 283805v JOURNAL  
Effect of salinity, temperature, and glucose on the production of *Vibrio*  
Page 8



FLAGELLI N10585880.txt

vulnificus hemolysin

AUTHOR(S): Kim, Hyun-Soo; Shin, Sung-Heui; Park, Hae-Ryoung; Lee, Shee-Eun; Kim, Choon-Mee; Kim, Soo-Young; Kim, Young-Ran; Lee, Hyun-Chul; Chung, Sun-Sik; Rhee, Joon-Haeng  
 LOCATION: Department of Microbiology, Chonnam National University Medical School, Kwangju, 501-746, S. Korea

JOURNAL: J. Bacteriol. Virol. (Journal of Bacteriology and Virology)

DATE: 2002 VOLUME: 32 NUMBER: 4 PAGES: 355-365 CODEN: JBVOAH ISSN: 1598-2467 LANGUAGE: English PUBLISHER: Journal of Bacteriology and Virology

7/3, K/5 (Item 3 from file: 399)

DI ALCG R) File 399: CA SEARCH(R)

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123006941 CA: 123(1)6941n JOURNAL

A study on the pathogenetic activity of the protease and hemolysin produced by *Vibrio vulnificus*. I. Biological properties of the hemolysin produced by *Vibrio vulnificus*

AUTHOR(S): Rhee, Joon-Haeng; Lee, Shee-Eun; Kwon, Hyung-Cheol; Chang, Heung-Shik; Ryu, Phil-Youl; Chung, Sun-Sik  
 LOCATION: Medical School, Chonnam National University, Kwangju, 501-190, S. Korea

JOURNAL: Taehan Msaengmul Hakhoechi DATE: 1994 VOLUME: 29 NUMBER: 5

PAGES: 381-98 CODEN: TMHCDX ISSN: 0253-3162 LANGUAGE: Korean

? E AU=KI M, SCO-YOUNG?

Ref	Items	Index-term
E1	216	AU=KI M SCO-YOUNG
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E3	0	*AU=KI M SCO-YOUNG?
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E5	4	AU=KI M SCO-YUN
E6	5	AU=KI M SCO-YUNG
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E9	1	AU=KI M SCO-OK
E10	1	AU=KI M SCO=CHU
E11	4	AU=KI M SCOAH
E12	1	AU=KI M SCOBANG CHANG

Enter P or PAGE for more

? S E1-E3

216	AU=KI M SCO-YOUNG
1	AU=KI M SCO-YOUNG DAVI D
0	AU=KI M SCO-YOUNG?

S8 217 E1-E3

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217	S8
369460	FLAG?
0	S8 AND FLAG?

? S S8 AND FLAGELLIN

217	S8
25810	FLAGELLIN
0	S8 AND FLAGELLIN

? S S8 AND (MUCOS? OR MUCCUS)

217	S8
1351917	MUCOS?
149469	MUCCUS

S11 2 S8 AND (MUCOS? OR MUCCUS)

? RD

FLAGELLIN0585880.txt

>>>Duplicate detection is not supported for File 393.

>>>Duplicate detection is not supported for File 391.

>>>Records from unsupported files will be retained in the RD set.

S12 1 RD (unique items)

? T S12/3, K/1

>>>KWC option is not available in file(s): 399

12/3, K/1 (Item 1 from file: 24)

DI ALCO(R) File 24: CSA Life Sciences Abstracts

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0003158407 IP ACCESSION NO: 7899305

*Vibrio vulnificus* metalloprotease VrpE is essentially required for swarming

Kim Choon-Mee; Park, Pa-Young; Chun, Ho-Jong; Kim Soo-Young;

Rhee, Joon-Haeng; Shin, Sung-Heui

Research Center for Resistant Cells, Chosun University Medical School,

Gwangju, Korea, [mailto:shsin@chosun.ac.kr]

FEMS Microbiology Letters, v 269, n 1, p 170-179, April 2007

PUBLICATION DATE: 2007

PUBLISHER: Elsevier Science, P.O. Box 211

DOCUMENT TYPE: Journal Article

RECORD TYPE: Abstract

LANGUAGE: English

SUMMARY LANGUAGE: English

ISSN: 0378-1097

FILE SEGMENT: Bacteriology Abstracts (Microbiology B)

Kim Choon-Mee; Park, Pa-Young; Chun, Ho-Jong; Kim Soo-Young;

Rhee, Joon-Haeng; Shin, Sung-Heui

? S FLAGELLIN AND VIBRIO

25610 FLAGELLIN

192950 VIBRIO

S13 764 FLAGELLIN AND VIBRIO

? S S13 AND TOLL(W) RECEPTOR

Processing

Processed 30 of 56 files ...

Completed processing all files

764 S13

175193 TOLL

7738302 RECEPTOR

2165 TOLL(W) RECEPTOR

S14 1 S13 AND TOLL(W) RECEPTOR

? T S14/3, K/1

>>>KWC option is not available in file(s): 399

14/3, K/1 (Item 1 from file: 399)

DI ALCO(R) File 399: CA SEARCH(R)

(c) 2009 American Chemical Society. All rts. reserv.

149217060 CA: 149(10)217060z PATENT

Modified flagellin with improved toll-like receptor 5 stimulating activity

INVENTOR(AUTHOR): Rhee, Joon Haeng; Lee, Shee Eun; Kim Soo Young

LOCATION: S. Korea

ASSIGNEE: Chonnam National University

PATENT: PCT International ; WO 200897016 A1 DATE: 20080814

APPLICATION: WO 2008KR709 (20080205) \*KR 13846 (20070209) \*KR 11330

(20080204)

PAGES: 35pp. CODEN: PI XXD2 LANGUAGE: English

PATENT CLASSIFICATIONS:

IPC/8 + Level Value Position Status Version Action Source Office:

C07K 0014/255 A I F B 20060101 H KR

DESIGNATED COUNTRIES: AE; AG; AL; AM; AO; AT; AU; AZ; BA; BB; BG; BH; BR; BY; BZ; CA; CH; CN; CO; CR; CU; CZ; DE; DK; DM; DO; DZ; EC; EE; EG; ES; FI; GB; GD; GE; GH; GM; GT; HN; HR; HU; ID; IL; IN; IS; JP; KE; KG; KM; KN; KP; KZ; LA; LC; LK; LR; LS; LT; LU; LY; MA; MD; ME; MG; MK; MN; MW; MX; MY; NA; NG; NI; NO; NZ; OM; PG; PH; PL; PT; RO; RS; RU; SC; SD; SE; SG; SK; SL; SM; SV; SY; TJ; TM; TR; TT; TZ DESIGNATED REG ONAL: AT; BE; BG; CH; CY; CZ; DE; DK; EE; ES; FI; FR; GB; GR; HR; HU; IE; IS; IT; LT; LU; LV; MD; MT; NL; NO; PL; PT; RO; SE; SI; SK; TR; BF; BJ; CF; CG; CI; CM; GA; GN; GQ; GW; ML; MR; NE; SN; TD; TG; BW; GH; GM; KE; LS; MW; MZ; NA; SD; SL; SZ; TZ; UG; ZM; ZW AM; AZ; BY; KG; KZ; MD; RU; TJ; TM

Set	Items	Description
S1	27	AU= RHEE, JOON-HAENG
S2	15	RD (unique items)
S3	0	S2 AND FLAGELLIN
S4	0	S2 AND FLAG?
S5	15	S2
S6	9	AU= LEE, SHEE-EUN
S7	5	RD (unique items)
S8	217	E1-E3
S9	0	S8 AND FLAG?
S10	0	S8 AND FLAGELLIN
S11	2	S8 AND (MUCOS? OR MUCCUS)
S12	1	RD (unique items)
S13	764	FLAGELLIN AND VIBRIO
S14	1	S13 AND TOLL(W RECEPTOR

Set	Items	Description
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E2	2	AU= RHEE, J- Y
E3	0	*AU= RHEE, J?
E4	2	AU= RHEE, JA
E5	2	AU= RHEE, JAE CHIN
E6	1	AU= RHEE, JAE HAN
E7	2	AU= RHEE, JAE HO
E8	4	AU= RHEE, JAE HUI
E9	1	AU= RHEE, JAE JIN
E10	4	AU= RHEE, JAE K
E11	37	AU= RHEE, JAE KEOL
E12	6	AU= RHEE, JAE KU

Enter P or PAGE for more  
 ? E AU= RHEE, JOON?

Ref	Items	Index-term
E1	25	AU= RHEE, JOON-SHI OK
E2	1	AU= RHEE, JOON-SHI K
E3	0	*AU= RHEE, JOON?
E4	1	AU= RHEE, JOONG E
E5	1	AU= RHEE, JOONG EUI
E6	1	AU= RHEE, JOONG GEUN
E7	1	AU= RHEE, JOONG HYUK
E8	2	AU= RHEE, JOONG EUI

E9 10 AU=RHEE, JCOONG-GEUN  
E10 6 AU=RHEE, JCOONG-SUP  
E11 2 AU=RHEE, JCOONG-YONG  
E12 2 AU=RHEE, JCONKYU

Enter P or PAGE for more  
? E AU=RHEE, JCON- HAENG

Ref	Items	Index-term
E1	8	AU=RHEE, JCON WHAN
E2	2	AU=RHEE, JCON WON
E3	27	*AU=RHEE, JCON- HAENG
E4	1	AU=RHEE, JCON- SEONG
E5	25	AU=RHEE, JCON- SHI OK
E6	1	AU=RHEE, JCON- SHI K
E7	1	AU=RHEE, JCOONG E
E8	1	AU=RHEE, JCOONG EUI
E9	1	AU=RHEE, JCOONG GEUN
E10	1	AU=RHEE, JCOONG HYUK
E11	2	AU=RHEE, JCOONG EUI
E12	10	AU=RHEE, JCOONG-GEUN

Enter P or PAGE for more  
? S E3  
S1 27 AU=RHEE, JCON- HAENG  
? RD

>>>Duplicate detection is not supported for File 393.

>>>Duplicate detection is not supported for File 391.

>>>Records from unsupported files will be retained in the RD set.

S2 15 RD (unique items)

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15 S2  
25810 FLAGELLIN  
S3 0 S2 AND FLAGELLIN

? S S2 AND FLAG?  
15 S2  
369460 FLAG?  
S4 0 S2 AND FLAG?

? S S2  
S5 15 S2

? T S5/3, K/1-5  
>>>KW C option is not available in file(s): 399

5/3, K/1 (Item 1 from file: 24)  
DI ALCG(R) File 24: CSA Life Sciences Abstracts  
(c) 2009 CSA. All rts. reserv.

0003663529 IP ACCESSI ON NO: 9163829  
The dysfunction and abnormal signaling pathway of dendritic cells loaded by tumor antigen can be overcome by neutralizing VEGF in multiple myeloma

Yang, Deok-Hwan; Park, Jung-Sun; Jin, Chun-Ji; Kang, Hyun-Kyu; Nam Jong-Hee; Rhee, Joon-Haeng; Kim Yeo-Kyeoung; Chung, Sang-Young; Choi, So-Jin-Na; Kim Hyeoung-Joon; Chung, Ik-Joo; Lee, Je-Jung  
Department of Hematology-Oncology, Chonnam National University Hwasun Hospital, Hwasun, Jeonnam, South Korea, [mailto:drjejung@honnam.ac.kr]

Leukemia Research, v 33, n 5, p 665-670, May 2009  
PUBLICATION DATE: 2009

FLAGELLI N10585880.txt

PUBLISHER: Elsevier Science, P. O. Box 800 Kidlington Oxford OX5 1DX UK,  
[mailto:nlinfo-f@elsevier.nl], [URL: <http://www.elsevier.nl>]

DOCUMENT TYPE: Journal Article  
RECORD TYPE: Abstract  
LANGUAGE: English  
SUMMARY LANGUAGE: English  
ISSN: 0145-2126  
FILE SEGMENT: Immunology Abstracts

Yang, Deok-Hwan; Park, Jung-Sun; Jin, Chun-Ji; Kang, Hyun-Kyu; Nam  
Jong-Hee; Rhee, Joon-Haeng; Kim Yeo-Kyeong; Chung, Sang-Young;  
Choi, So-Jin-Na; Kim Hyeoung-Joon...

5/3, K/2 (Item 2 from file: 24)  
DI ALCOR File 24: CSA Life Sciences Abstracts  
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0003522208 IP ACCESSION NO: 7041018  
Vibrio vulnificus Vulnibactin, But Not Metalloprotease VvpE, Is Essentially  
Required for Iron Uptake from Human Holotransferrin

Kim Choon-Mee; Park, Ra-Young; Park, Jeong-Hee; Sun, Hui-Yu; Bai,  
Young-Hoon; Ryu, Phil-Yeol; Kim Soo-Young; Rhee, Joon-Haeng;  
Shin, Sung-Heui  
Research Center for Resistant Cells, Chosun University Medical School;  
Gwangju 501-759, South Korea, [mailto:shsin@chosun.ac.kr]

Biological & Pharmaceutical Bulletin, v 29, n 5, p 911-918, May 2006  
PUBLICATION DATE: 2006

DOCUMENT TYPE: Journal Article  
RECORD TYPE: Abstract  
LANGUAGE: English  
SUMMARY LANGUAGE: English  
ISSN: 0918-6158  
ASFA NO: CS0728831  
FILE SEGMENT: Bacteriology Abstracts (Microbiology B)  
...Park, Jeong-Hee; Sun, Hui-Yu; Bai, Young-Hoon; Ryu, Phil-Yeol; Kim  
Soo-Young; Rhee, Joon-Haeng; Shin, Sung-Heui

5/3, K/3 (Item 3 from file: 24)  
DI ALCOR File 24: CSA Life Sciences Abstracts  
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0003520430 IP ACCESSION NO: 6434094  
Inactivation of Vibrio vulnificus Hemolysin by Dimerization but Not  
Proteolysis

Shin, Sung-Heui; Sun, Hui-Yu; Choi, M-Hwa; Park, Ra-Young; Bai,  
Young-Hoon; Kim Choon-Mee; Kim Soo-Young; Kim Young-Ran; Lee,  
Shae-Eun; Rhee, Joon-Haeng  
Research Center for Resistant Cells, Chosun University Medical School

Biological & Pharmaceutical Bulletin, v 28, n 7, 2005  
PUBLICATION DATE: 2005

PUBLISHER: Pharmaceutical Society of Japan, 2-12-15, Shibuya Shibuya-ku  
Tokyo 150-0002 Japan, [mailto:ronb@pharm.or.jp],  
[URL: <http://bbp.pharm.or.jp>]

DOCUMENT TYPE: Journal Article

RECORD TYPE: Abstract

LANGUAGE: English

SUMMARY LANGUAGE: English

ISSN: 0918-6158

FILE SEGMENT: Bacteriology Abstracts (Microbiology B)

...Bai, Young-Hoon; Kim Choon-Mee; Kim Soo-Young; Kim Young-Ran;  
Lee, Shee-Eun; Rhee, Joon-Haeng

5/3, K/4 (Item 4 from file: 24)  
DIALOG File 24: CSA Life Sciences Abstracts  
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0003158407 I P ACCESSION NO: 7899305  
Vibrio vulnificus metalloprotease VvpE is essentially required for swarming

Kim Choon-Mee; Park, Ra-Young; Chun, Ho-Jong; Kim Soo-Young; Rhee,  
Joon-Haeng; Shin, Sung-Heui  
Research Center for Resistant Cells, Chosun University Medical School,  
Gwangju, Korea, [mailto:shsin@chosun.ac.kr]

FEMS Microbiology Letters, v 269, n 1, p 170-179, April 2007  
PUBLICATION DATE: 2007

PUBLISHER: Elsevier Science, P.O. Box 211

DOCUMENT TYPE: Journal Article

RECORD TYPE: Abstract

LANGUAGE: English

SUMMARY LANGUAGE: English

ISSN: 0378-1097

FILE SEGMENT: Bacteriology Abstracts (Microbiology B)

Kim Choon-Mee; Park, Ra-Young; Chun, Ho-Jong; Kim Soo-Young; Rhee,  
Joon-Haeng; Shin, Sung-Heui

5/3, K/5 (Item 1 from file: 393)  
DIALOG File 393: Beilstein Database - Abstracts  
(c) 2008 Beilstein GmbH. All rights reserved.

Beilstein Abstract Id: 6553384

Title: Vibrio vulnificus Vulnibactin, But Not Metalloprotease VvpE, Is  
Essentially Required for Iron Uptake from Human Holotransferrin

Document Type: Journal Record Type: Abstract

Author: Kim Choon-Mee; Park, Ra-Young; Park, Jeong-Hee; Sun, Hui-Yu;  
Bai, Young-Hoon; Ryu, Phil-Yeol; Kim Soo-Young; Rhee,

Joon-Haeng; Shin, Sung-Heui

Citation: Biol. Pharm. Bull. (2006) Series: 29-5, 911 - 918 CODEN:

BPBLEO Language: English

Abstract Language: English

... Author: Park, Jeong-Hee; Sun, Hui-Yu; Bai, Young-Hoon; Ryu,  
Phil-Yeol; Kim Soo-Young; Rhee, Joon-Haeng; Shin,  
Sung-Heui

? DS

Set	Items	Description
S1	27	ALL RHEE, JOON-HAENG
S2	15	RD (unique items)
S3	0	S2 AND FLAGELLIN

S4 0 S2 AND FLAG?

S5 15 S2

? T S5/3, K/6-15

>>>KWIC option is not available in file(s): 399

5/3, K/6 (Item 2 from file: 393)  
DIALOG(R) File 393: Beilstein Database - Abstracts  
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Beilstein Abstract Id: 6505604  
Title: Inactivation of *Vibrio vulnificus* hemolysin by oligomerization but not proteolysis  
Document Type: Journal Record Type: Abstract  
Author: Shin, Sung-Heui; Sun, Hui-Yu; Choi, M-Hwa; Park, Ra-Young; Bai, Young-Hoon; Kim Choon-Mee; Kim Soo-Young; Kim Young-Ran; Lee, Shee-Eun; Rhee, Joon-Haeng  
Citation: Biol. Pharm. Bull. (2005) Series: 28-7, 1294 - 1297 CODEN: BPBLEO Language: English  
Abstract Language: English

... Author: Bai, Young-Hoon; Kim Choon-Mee; Kim Soo-Young; Kim Young-Ran; Lee, Shee-Eun; Rhee, Joon-Haeng

5/3, K/7 (Item 1 from file: 399)  
DIALOG(R) File 399: CA SEARCH(R)  
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148260207 CA: 148(12)260207u JOURNAL  
Induction of multiple myeloma-specific cytotoxic T lymphocyte stimulation by dendritic cell pulsing with purified and optimized myeloma cell lysates  
AUTHOR(S): Lee, Je-Jung; Choi, Bo-Hwa; Kang, Hyun-Kyu; Park, Myong-Suk; Park, Jung-Sun; Kim Sang-Ki; Pham Thanh-Nhan Nguyen; Cho, Duck; Nam Jong-Hee; Kim Young-Jin; Rhee, Joon-Haeng; Yang, Deok-Hwan; Kim Yeo-Kyeoung; Kim Hyeoung-Joon; Chung, Ik-Joo  
LOCATION: Clinical Vaccine R&D Center, Chonnam National University, Department of Hematology - Oncology, Chonnam National University Hwasun Hospital, Jeonnam, S. Korea  
JOURNAL: Leuk. Lymphoma (Leukemia & Lymphoma) DATE: 2007 VOLUME: 48  
NUMBER: 10 PAGES: 2022-2031 CODEN: LELYEA ISSN: 1042-8194 LANGUAGE: English PUBLISHER: Informa Healthcare

5/3, K/8 (Item 2 from file: 399)  
DIALOG(R) File 399: CA SEARCH(R)  
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146498196 CA: 146(25)498196y JOURNAL  
Down-regulation of cellular vascular endothelial growth factor levels induces differentiation of leukemic cells to functional leukemic dendritic cells in acute myeloid leukemia  
AUTHOR(S): Kang, Hyun-Kyu; Park, Jung-Sun; Kim Sang-Ki; Choi, Bo-Hwa; Pham Thanh-Nhan Nguyen; Zhu, Xiao-Wei; Cho, Duck; Nam Jong-Hee; Kim Young-Jin; Rhee, Joon-Haeng; Chung, Ik-Joo; Kim Hyeoung-Joon; Lee, Je-Jung  
LOCATION: Department of Hematology-Oncology, Chonnam National University Medical School, Gwangju, S. Korea  
JOURNAL: Leuk. Lymphoma (Leukemia & Lymphoma) DATE: 2006 VOLUME: 47  
NUMBER: 10 PAGES: 2224-2233 CODEN: LELYEA ISSN: 1042-8194 LANGUAGE: English PUBLISHER: Informa Healthcare

DI ALCOG(R) File 399: CA SEARCH(R)

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146224476 CA: 146(12)224476f JOURNAL

X-gal inhibits the swarming of *Vibrio* species

AUTHOR(S): Kim, Moon-Young; Park, Ra-Young; Bai, Young-Hoon; Chung, Yoon-Young; Kim Choon-Mee; Kim Soo-Young; Rhee, Joon-Haeng; Shin, Sung-Heui

LOCATION: Research Center for Resistant Cells, Chosun University Medical School, Gwangju, 501-759, S. Korea

JOURNAL: J. Microbiol. Methods (Journal of Microbiological Methods)

DATE: 2006 VOLUME: 66 NUMBER: 3 PAGES: 552-555 CODEN: JMDQ ISSN: 0167-7012 PUBLISHER: ELSEVIER B.V. 0167-7012(06)00018-2 LANGUAGE: English

PUBLISHER: Elsevier B.V.

5/3, K/10 (Item 4 from file: 399)

DI ALCOG(R) File 399: CA SEARCH(R)

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146077702 CA: 146(5)77702w JOURNAL

Swarming differentiation of *Vibrio vulnificus* downregulates the expression of the *vvhBA* hemolysin gene via the *LuxS* quorum-sensing system

AUTHOR(S): Kim, Moon-Young; Park, Ra-Young; Choi, M-Hwa; Sun, Hui-Yu; Kim Choon-Mee; Kim Soo-Young; Rhee, Joon-Haeng; Shin, Sung-Heui

LOCATION: Research Center for Resistant Cells, Chosun University Medical School, Gwangju, 501-759, S. Korea

JOURNAL: J. Microbiol. (Seoul, Repub. Korea) (Journal of Microbiology)

(Seoul, Republic of Korea) DATE: 2006 VOLUME: 44 NUMBER: 2 PAGES: 226-232 CODEN: JOMFG ISSN: 1225-8873 LANGUAGE: English PUBLISHER: Microbiological Society of Korea

5/3, K/11 (Item 5 from file: 399)

DI ALCOG(R) File 399: CA SEARCH(R)

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145203874 CA: 145(11)203874y JOURNAL

Effect of the *crp* mutation on the utilization of transferrin-bound iron by *Vibrio vulnificus*

AUTHOR(S): Choi, M-Hwa; Sun, Hui-Yu; Park, Ra-Young; Kim Choon-Mee; Bai, Young-Hoon; Kim Young-Ran; Rhee, Joon-Haeng; Shin, Sung-Heui

LOCATION: Research Center for Resistant Cells, Chosun University Medical School, Gwangju, S. Korea

JOURNAL: FEMS Microbiol. Lett. (FEMS Microbiology Letters) DATE: 2006

VOLUME: 257 NUMBER: 2 PAGES: 285-292 CODEN: FMED7 ISSN: 0378-1097 LANGUAGE: English PUBLISHER: Blackwell Publishing Ltd.

5/3, K/12 (Item 6 from file: 399)

DI ALCOG(R) File 399: CA SEARCH(R)

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145060561 CA: 145(4)60561f JOURNAL

Suppression and inactivation of *Vibrio vulnificus* hemolysin in cirrhotic ascites, a human *ex vivo* experimental system

AUTHOR(S): Choi, M-Hwa; Park, Ra-Young; Sun, Hui-Yu; Kim Choon-Mee; Bai, Young-Hoon; Lee, Shee-Eun; Kim Soo-Young; Kim Young-Ran; Rhee, Joon-Haeng; Shin, Sung-Heui

LOCATION: Research Center for Resistant cells, Chosun University Medical School, Gwangju, S. Korea

JOURNAL: FEMS Immunol. Med. Microbiol. (FEMS Immunology and Medical

Microbiology) DATE: 2006 VOLUME: 47 NUMBER: 2 PAGES: 226-232 CODEN: FEMS



FIM EV ISSN: 0928-8244 LANGUAGE: English PUBLISHER: Blackwell Publishing Ltd.

5/3, K/13 (Item 7 from file: 399)

DIALOG(R) File 399: CA SEARCH(R)

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143244771 CA: 143(14)244771q JOURNAL

Vibrio vulnificus metalloprotease VvpE has no direct effect on the iron-assimilation from human holotransferrin

AUTHOR(S): Shin, Sung-Heui; Sun, Hui-Yu; Park, Ra-Young; Kim Choon-Mee; Kim Soo-Young; Rhee, Joon-Haeng

LOCATION: Research Center for Resistant Cells, Department of Microbiology, Chosun University Medical School, Gwangju, 501-759, S. Korea

JOURNAL: FEMS Microbiol. Lett. (FEMS Microbiology Letters) DATE: 2005

VOLUME: 247 NUMBER: 2 PAGES: 221-229 CODEN: FMLED7 ISSN: 0378-1097

PUBLISHER ITEM IDENTIFIER: 0378-1097(05)00297-1 LANGUAGE: English

PUBLISHER: Elsevier B.V.

5/3, K/14 (Item 8 from file: 399)

DIALOG(R) File 399: CA SEARCH(R)

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138283805 CA: 138(19)283805v JOURNAL

Effect of salinity, temperature, and glucose on the production of Vibrio vulnificus hemolysin

AUTHOR(S): Kim Hyun-Soo; Shin, Sung-Heui; Park, Hae-Ryoung; Lee, Shee-Eun; Kim Choon-Mee; Kim Soo-Young; Kim Young-Ran; Lee, Hyun-Chul; Chung, Sun-Sik; Rhee, Joon-Haeng

LOCATION: Department of Microbiology, Chonnam National University Medical School, Kwangju, 501-746, S. Korea

JOURNAL: J. Bacteriol. Virol. (Journal of Bacteriology and Virology)

DATE: 2002 VOLUME: 32 NUMBER: 4 PAGES: 355-365 CODEN: JBVOAH ISSN:

1598-2467 LANGUAGE: English PUBLISHER: Journal of Bacteriology and Virology

5/3, K/15 (Item 9 from file: 399)

DIALOG(R) File 399: CA SEARCH(R)

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123006941 CA: 123(1)6941n JOURNAL

A study on the pathogenetic activity of the protease and hemolysin produced by Vibrio vulnificus. I. Biological properties of the hemolysin produced by Vibrio vulnificus

AUTHOR(S): Rhee, Joon-Haeng; Lee, Shee-Eun; Kwon, Hyung-Cheol; Chang, Heung-Shik; Ryu, Phil-Youl; Chung, Sun-Sik  
LOCATION: Medical School, Chonnam National University, Kwangju, 501-190, S. Korea

JOURNAL: Taehan M saengmul Hakhoechi DATE: 1994 VOLUME: 29 NUMBER: 5

PAGES: 381-98 CODEN: TMHODX ISSN: 0253-3162 LANGUAGE: Korean

? E AU=LEE, SHEE-EUN

Ref	Items	Index-term
E1	9	*AU=LEE, SHEE-EUN
E2	1	AU=LEE, SHEE-NA
E3	3	AU=LEE, SHEE-YONG
E4	1	AU=LEE, SHEEN-WOO
E5	2	AU=LEE, SHEEN-JE
E6	1	AU=LEE, SHEEN-MOK
E7	11	AU=LEE, SHEEN-WOO

E8 11 AU=LEE, SHEENA  
E9 1 AU=LEE, SHEENA R  
E10 2 AU=LEE, SHEENA R  
E11 13 AU=LEE, SHEEYONG  
E12 4 AU=LEE, SHEE YEN

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? S E1  
S6 9 AU= LEE, SHEE-EUN  
? RD

>>>Duplicate detection is not supported for File 393.

>>>Duplicate detection is not supported for File 391.

>>>Records from unsupported files will be retained in the RD set.

S7 5 RD (unique items)  
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>>>KWC option is not available in file(s): 399

7/3, K/1 (Item 1 from file: 24)  
DIALCOG(R) File 24: CSA Life Sciences Abstracts  
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0003520430 IP ACCESSION NO: 6434094  
Inactivation of *Vibrio vulnificus* Hemolysin by Oligomerization but Not  
Proteolysis

Shin, Sung-Heui; Sun, Hui-Yu; Choi, M-Hwa; Park, Ra-Young; Bai,  
Young-Hoon; Kim Choon-Mee; Kim Soo-Young; Kim Young-Ran; Lee,  
Shee-Eun; Rhee, Joon-Haeng  
Research Center for Resistant Cells, Chosun University Medical School

Biological & Pharmaceutical Bulletin, v 28, n 7, 2005  
PUBLICATION DATE: 2005

PUBLISHER: Pharmaceutical Society of Japan, 2-12-15, Shibuya Shibuya-ku  
Tokyo 150-0002 Japan, [mailto:ronb@pharm.or.jp],  
[URL: http://bpb.pharm.or.jp]

DOCUMENT TYPE: Journal Article  
RECORD TYPE: Abstract  
LANGUAGE: English  
SUMMARY LANGUAGE: English  
ISSN: 0918-6158  
FILE SEGMENT: Bacteriology Abstracts (Microbiology B)

...Park, Ra-Young; Bai, Young-Hoon; Kim Choon-Mee; Kim Soo-Young;  
Kim Young-Ran; Lee, Shee-Eun; Rhee, Joon-Haeng

7/3, K/2 (Item 1 from file: 393)  
DIALCOG(R) File 393: Beilstein Database - Abstracts  
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Beilstein Abstract Id: 6505604  
Title: Inactivation of *Vibrio vulnificus* hemolysin by oligomerization but  
not proteolysis  
Document Type: Journal Record Type: Abstract  
Author: Shin, Sung-Heui; Sun, Hui-Yu; Choi, M-Hwa; Park, Ra-Young;  
Bai, Young-Hoon; Kim Choon-Mee; Kim Soo-Young; Kim Young-Ran  
; Lee, Shee-Eun; Rhee, Joon-Haeng  
Citation: Biol. Pharm. Bull. (2005) Series: 28-7, 1294 - 1297 CODEN:

BPBLO Language: English

Abstract Language: English

... Author: Park, Ra-Young; Bai, Young-Hoon; Kim Choon-Mee; Kim  
Soo-Young; Kim Young-Ran; Lee, Shee-Eun; Rhee,  
Joon-Haeng

7/3, K/3 (Item 1 from file: 399)

DI ALCOG R File 399: CA SEARCH R

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145060561 CA: 145(4) 60561f JOURNAL

Suppression and inactivation of *Vibrio vulnificus* hemolysin in cirrhotic  
ascites, a human ex vivo experimental system

AUTHOR(S): Choi, M-Hwa; Park, Ra-Young; Sun, Hui-Yu; Kim Choon-Mee;

Bai, Young-Hoon; Lee, Shee-Eun; Kim Soo-Young; Kim Young-Ran; Rhee,

Joon-Haeng; Shin, Sung-Heui

LOCATION: Research Center for Resistant cells, Chosun University Medical  
School, Gwangju, S. KoreaJOURNAL: FEMS Immunol. Med. Microbiol. (FEMS Immunology and Medical  
Microbiology) DATE: 2006 VOLUME: 47 NUMBER: 2 PAGES: 226-232 CODEN:  
MIM EV ISSN: 0928-8244 LANGUAGE: English PUBLISHER: Blackwell Publishing  
Ltd.

7/3, K/4 (Item 2 from file: 399)

DI ALCOG R File 399: CA SEARCH R

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138283805 CA: 138(19) 283805v JOURNAL

Effect of salinity, temperature, and glucose on the production of *Vibrio*  
*vulnificus* hemolysinAUTHOR(S): Kim Hyun-Soo; Shin, Sung-Heui; Park, Hae-Ryoung; Lee,  
Shee-Eun; Kim Choon-Mee; Kim Soo-Young; Kim Young-Ran; Lee, Hyun-Chul;  
Chung, Sun-Sik; Rhee, Joon-HaengLOCATION: Department of Microbiology, Chonnam National University Medical  
School, Kwangju, 501-746, S. Korea

JOURNAL: J. Bacteriol. Virol. (Journal of Bacteriology and Virology)

DATE: 2002 VOLUME: 32 NUMBER: 4 PAGES: 355-365 CODEN: JBV OAH ISSN:  
1598-2467 LANGUAGE: English PUBLISHER: Journal of Bacteriology and  
Virology

7/3, K/5 (Item 3 from file: 399)

DI ALCOG R File 399: CA SEARCH R

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123006941 CA: 123(1) 6941n JOURNAL

A study on the pathogenetic activity of the protease and hemolysin  
produced by *Vibrio vulnificus*. I. Biological properties of the hemolysin  
produced by *Vibrio vulnificus*AUTHOR(S): Rhee, Joon-Haeng; Lee, Shee-Eun; Kwon, Hyung-Cheol; Chang,  
Heung-Shik; Ryu, Phil-Youl; Chung, Sun-SikLOCATION: Medical School, Chonnam National University, Kwangju, 501-190,  
S. Korea

JOURNAL: Taehan M saengmul Hakhoechi DATE: 1994 VOLUME: 29 NUMBER: 5

PAGES: 381-98 CODEN: TMHC DX ISSN: 0253-3162 LANGUAGE: Korean

? E AU=KIM SOO-YOUNG?

Ref Items Index-term

E1 216 AU=KIM SOO-YOUNG

E2 1 AU=KIM SOO-YOUNG DAVID

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E3      0  *AU=KI M  SCO-YOUNG?
E4      1  AU=KI M  SCO-YUL
E5      4  AU=KI M  SCO-YUN
E6      5  AU=KI M  SCO-YUNG
E7      1  AU=KI M  SCO-ZI
E8      11 AU=KI M  SCO-ZIN
E9      1  AU=KI M  SCO-OK
E10     1  AU=KI M  SCO-CHU
E11     4  AU=KI M  SCO-AH
E12     1  AU=KI M  SCOBANG-CHANG

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Enter P or PAGE for more

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? S E1-E3
      216 AU=KI M  SCO-YOUNG
      1  AU=KI M  SCO-YOUNG DAVI D
      0  AU=KI M  SCO-YOUNG?
S8      217 E1-E3
? S S8 AND FLAG?
      217 S8
      369460 FLAG?
S9      0  S8 AND FLAG?
? S S8 AND FLAGELLI N
      217 S8
      25810 FLAGELLI N
S10     0  S8 AND FLAGELLI N
? S S8 AND (MUCCS? OR MUCCUS)
      217 S8
      1351917 MUCCS?
      149469 MUCCUS
S11     2  S8 AND (MUCCS? OR MUCCUS)
? RD

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>>>Duplicate detection is not supported for File 393.

>>>Duplicate detection is not supported for File 391.

>>>Records from unsupported files will be retained in the RD set.

S12 1 RD (unique items)

? T S12/3, K/1

>>>KWC option is not available in file(s): 399

12/3, K/1 (Item 1 from file: 24)  
 DIALOG(R) File 24: CSA Life Sciences Abstracts  
 (c) 2009 CSA. All rts. reserv.

0003158407 IP ACCESSION NO: 7899305  
 Vibrio vulnificus metalloprotease VrpE is essentially required for swarming

Kim Choon-Mee; Park, Ra-Young; Chun, Ho-Jong; Kim Soo-Young;  
 Rhee, Joon-Haeng; Shin, Sung-Heui  
 Research Center for Resistant Cells, Chosun University Medical School,  
 Gwangju, Korea, [mailto:shsin@chosun.ac.kr]

FEMS Microbiology Letters, v 269, n 1, p 170-179, April 2007  
 PUBLICATION DATE: 2007

PUBLISHER: Elsevier Science, P.O. Box 211

DOCUMENT TYPE: Journal Article  
 RECORD TYPE: Abstract  
 LANGUAGE: English  
 SUMMARY LANGUAGE: English  
 ISSN: 0378-1097

FILE SEGMENT: Bacteriology Abstracts (Microbiology B)

Kim Choon-Mee; Park, Ra-Young; Chun, Ho-Jong; Kim Soo-Young;  
Rhee, Joon-Haeng; Shin, Sung-Heui

? S FLAGELLIN AND VI BRI O

25610 FLAGELLIN

192950 VI BRI O

S13 764 FLAGELLIN AND VI BRI O

? S S13 AND TOLL(W RECEPTOR

Processing

Processed 30 of 56 files ...

Completed processing all files

764 S13

175193 TOLL

7738302 RECEPTOR

2165 TOLL(W RECEPTOR

S14 1 S13 AND TOLL(W RECEPTOR

? T S14/3, K/1

&gt;&gt;&gt;KWC option is not available in file(s): 399

14/3, K/1 (Item 1 from file: 399)

DI ALCO (R) File 399: CA SEARCH (R)

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149217060 CA: 149(10)217060z PATENT

Modified flagellin with improved toll-like receptor 5 stimulating  
activity

INVENTOR(AUTHOR): Rhee, Joon Haeng; Lee, Shee Eun; Kim Soo Young

LOCATION: S. Korea

ASSIGNEE: Chonnam National University

PATENT: PCT International ; WO 200897016 A1 DATE: 20080814

APPLICATI ON: WO 2008KR709 (20080205) \*KR 13846 (20070209) \*KR 11330  
(20080204)

PAGES: 35pp. CODEN: PIXXD2 LANGUAGE: English

PATENT CLASSIFICATIONS:

IPC/8 + Level Value Position Status Version Action Source Office:

C07K 0014/255 A I F B 20060101 H KR

DESIGNATED COUNTRIES: AE; AG; AL; AM; AO; AT; AU; AZ; BA; BB; BG; BH; BR;  
 BW; BY; BZ; CA; CH; CN; CO; CR; CU; CZ; DE; DK; DM; DO; DZ; EC; EE; EG; ES;  
 FI; GB; GD; GE; GH; GM; GT; HN; HR; HU; ID; IL; IN; IS; JP; KE; KG; KM; KN;  
 KP; KZ; LA; LC; LK; LR; LS; LT; LU; LY; MA; MD; ME; MG; MK; MN; MW; MX; MY;  
 MZ; NA; NG; NI; NO; NZ; OM; PG; PH; PL; PT; RO; RS; RU; SC; SD; SE; SG; SK;  
 SL; SM; SV; SY; TJ; TM; TN; TR; TT; TZ DESIGNATED REGIONAL: AT; BE; BG; CH;  
 CY; CZ; DE; DK; EE; ES; FI; FR; GB; GR; HR; HU; IE; IS; IT; LT; LU; LV;  
 MC; MT; NL; NO; PL; PT; RO; SE; SI; SK; TR; BF; BJ; CF; CG; CI; CM; GA; GN;  
 GQ; GW; ML; MR; NE; SN; TD; TG; BW; GH; GM; KE; LS; MW; MZ; NA; SD; SL; SZ;  
 TZ; UG; ZM; ZW AM; AZ; BY; KG; KZ; MD; RU; TJ; TM

? DS

Set	Items	Description
S1	27	AU- RHEE, JOON-HAENG
S2	15	RD (unique items)
S3	0	S2 AND FLAGELLIN
S4	0	S2 AND FLAG?
S5	15	S2
S6	9	AU- LEE, SHEE-EUN
S7	5	RD (unique items)
S8	217	E1-E3
S9	0	S8 AND FLAG?
S10	0	S8 AND FLAGELLIN
S11	2	S8 AND (MUCOS? OR MUCCOUS)
S12	1	RD (unique items)
S13	764	FLAGELLIN AND VI BRI O

S14 1 S13 AND TOLL(W RECEPTOR  
 ? DS

Set	Items	Description
S1	27	AU= FHEE, JOON-HAENG
S2	15	RD (unique items)
S3	0	S2 AND FLAGELLIN
S4	0	S2 AND FLAG?
S5	15	S2
S6	9	AU= LEE, SHEE-EUN
S7	5	RD (unique items)
S8	217	E1-E3
S9	0	S8 AND FLAG?
S10	0	S8 AND FLAGELLIN
S11	2	S8 AND (MUCOS? OR MUCCUS)
S12	1	RD (unique items)
S13	764	FLAGELLIN AND VIBRIO
S14	1	S13 AND TOLL(W RECEPTOR
? S S13 AND (IMMUN? OR ADJUVANT OR STIMUL?)		
Processing		
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Processing		
Processed	20 of	56 files ...
Processing		
Processed	40 of	56 files ...
Processing		
Completed processing all files		
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	17597612	IMMUN?
	680381	ADJUVANT
	8317022	STIMUL?
	S15 290	S13 AND (IMMUN? OR ADJUVANT OR STIMUL?)
? S S15 AND (RESPONSE)		
	290	S15
	13742212	RESPONSE
	S16 85	S15 AND (RESPONSE)
? RD		

>>>Duplicate detection is not supported for File 393.

>>>Duplicate detection is not supported for File 391.

>>>Records from unsupported files will be retained in the RD set.

S17 41 RD (unique items)  
 ? S S17 AND VULNIFOCUS  
 41 S17  
 16828 VULNIFOCUS  
 S18 10 S17 AND VULNIFOCUS  
 ? RD

>>>Duplicate detection is not supported for File 393.

>>>Duplicate detection is not supported for File 391.

>>>Records from unsupported files will be retained in the RD set.

S19 10 RD (unique items)  
 ? T S19/3, K/1-10  
 >>>KWC option is not available in file(s): 399

0020850964 BIOSIS NO.: 200900191298  
 Effect of the Heat Shock Protein 70 Contamination on the Mucosal  
 Adjuvant Activity of Recombinant Bacterial Flagellin  
 AUTHOR: Kim S Y (Reprint); Tran T X; Nguyen T C; Bae S J; Lee S E; Rhee J H  
 AUTHOR ADDRESS: Chonnam Natl Univ, Sch Med, Kwangju, South Korea\*\*South  
 Korea  
 JOURNAL: Abstracts of the General Meeting of the American Society for  
 Microbiology 108 p256 2008 2008  
 CONFERENCE/MEETING: 108th General Meeting of the  
 American-Society-for-Microbiology Boston, MA, USA June 01 -05, 2008;  
 20080601  
 SPONSOR: Amer Soc Microbiol  
 ISSN: 1060-2011  
 DOCUMENT TYPE: Meeting; Meeting Abstract  
 RECORD TYPE: Citation  
 LANGUAGE: English

Effect of the Heat Shock Protein 70 Contamination on the Mucosal  
 Adjuvant Activity of Recombinant Bacterial Flagellin

DESCRIPTORS:

...ORGANISMS: *Vibrio vulnificus* (Vibrionaceae)  
 CHEMICALS & BIOCHEMICALS: ...recombinant bacterial flagellin;  
 METHODS & EQUIPMENT: immunization-  
 MISCELLANEOUS TERMS: immune response; ...

...adjuvant activity

CONCEPT CODES:

19/3,K/2 (Item 2 from file: 5)  
 DIALOG(R) File 5: Biosis Previews(R)  
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0020189834 BIOSIS NO.: 200800236773  
 A bacterial flagellin, *Vibrio vulnificus* FlaB, has a  
 strong mucosal adjuvant activity to induce protective  
 immunity  
 AUTHOR: Lee S (Reprint); Kim S; Jeong B; Kim Y; Bae S; Choy H; Chung S;  
 Rhee J  
 AUTHOR ADDRESS: Genome Res Ctr Enteropathogen Bacteria, Res Inst Vibrio  
 Infect, Kwangju, South Korea\*\*South Korea  
 JOURNAL: Abstracts of the General Meeting of the American Society for  
 Microbiology 105 p252 2005 2005  
 CONFERENCE/MEETING: 105th General Meeting of the  
 American-Society-for-Microbiology Atlanta, GA, USA June 05 -09, 2005;  
 20050605  
 SPONSOR: Amer Soc Microbiol  
 ISSN: 1060-2011  
 DOCUMENT TYPE: Meeting; Meeting Poster  
 RECORD TYPE: Citation  
 LANGUAGE: English

A bacterial flagellin, *Vibrio vulnificus* FlaB, has a  
 strong mucosal adjuvant activity to induce protective  
 immunity

DESCRIPTORS:

...MAJOR CONCEPTS: Immune System  
 ORGANISMS: *Vibrio vulnificus* (Vibrionaceae)  
 CHEMICALS & BIOCHEMICALS:  
 MISCELLANEOUS TERMS: immune response;

CONCEPT CODES:

19/3, K/3 (Item 3 from file: 5)  
 DIALOG(R) File 5: Biosis Previews(R)  
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0020142049 BIOSIS NO.: 200800188988  
 A chimera of flagellin and cholera toxin as a mucosal adjuvant  
 AUTHOR: Kim S Y (Reprint); Lee S E; Vo T D H; Bae S J; Kim K; Phee J H  
 AUTHOR ADDRESS: Chonnam Natl Univ, Sch Med, Clin Vaccine R and D Ctr,  
 Kwangju, South Korea\*\*South Korea  
 JOURNAL: Abstracts of the General Meeting of the American Society for  
 Microbiology 107 p287 2007 2007  
 CONFERENCE/MEETING: 107th General Meeting of the  
 American Society for Microbiology Toronto, CANADA 2007,  
 SPONSOR: Amer Soc Microbiol  
 ISSN: 1060-2011  
 DOCUMENT TYPE: Meeting; Meeting Abstract  
 RECORD TYPE: Citation  
 LANGUAGE: English

A chimera of flagellin and cholera toxin as a mucosal adjuvant  
 DESCRIPTORS:

...MAJOR CONCEPTS: Immune System  
 ORGANISMS: *Vibrio vulnificus* (Vibrionaceae)  
 CHEMICALS & BIOCHEMICALS: ...flagellin; ...  
 ...immunologic-drug, toxicity...  
 ...immunologic-drug, toxicity  
 MISCELLANEOUS TERMS: protective immunity; ...  
 ...systemic immune response; ...  
 ...immunogenicity; ...  
 ...mucosal immune response; ...  
 ...mucosal adjuvant activity  
 CONCEPT CODES:

19/3, K/4 (Item 1 from file: 34)  
 DIALOG(R) File 34: SciSearch(R) Cited Ref Sci  
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14119785 Genuine Article#: 943FI No. References: 38  
 Title: Induction of interleukin-8 production via nuclear factor-kappa B  
 activation in human intestinal epithelial cells infected with  
*Vibrio vulnificus*  
 Author(s): Lee BC; Kim SH; Choi SH; Kim TS (REPRINT)  
 Corporate Source: Chonnam Natl Univ, Coll Pharm Dept Pharm Kwangju  
 500757//South Korea/ (REPRINT); Chonnam Natl Univ, Coll Pharm Dept  
 Pharm Kwangju 500757//South Korea/; Seoul Natl Univ, Sch Agr Biotechnol,  
 Dept Food Sci & Technol, Seoul//South Korea/(taekim@chonnam.ac.kr)  
 Journal: IMMUNOLOGY, 2005, V115, N4 (AUG), P506-515  
 ISSN: 0019-2805 Publication date: 20050800  
 Publisher: BLACKWELL PUBLISHING, 9600 GARSINGTON RD, OXFORD OX4 2DQ, OXON,  
 ENGLAND  
 Language: English Document Type: ARTICLE (ABSTRACT AVAILABLE)

...Title: 8 production via nuclear factor-kappa B activation in human  
 intestinal epithelial cells infected with *Vibrio vulnificus*  
 Abstract: *Vibrio vulnificus*, a Gram-negative estuarine  
 bacterium is a causative agent of food-borne diseases, such as  
 Page 24



FLAGELLIN010585880.txt

life-threatening septicemia and wound infection disease. *V. vulnificus* penetrating into the epithelial barrier stimulates an inflammatory response in the adjacent mucosa. Therefore, interaction between *V. vulnificus* and epithelial cells is important for understanding of both the immunology of mucosal surfaces and *V. vulnificus*. In this study, we investigated the effect and action mechanism of *V. vulnificus* infection on production of interleukin (IL)-8, a proinflammatory cytokine, in human intestinal epithelial INT-407 cells. *V. vulnificus* infection significantly induced IL-8 production in a time- and multiplicity of infection (MOI)-dependent manner, as determined by human IL-8 enzyme-linked immunosorbent assay (ELISA). In addition, *V. vulnificus* infection significantly increased IL-8 mRNA levels in INT-407 cells, indicating that the increased IL-8 production by *V. vulnificus* occurred at the transcriptional level. *V. vulnificus* infection also enhanced IL-8 gene promoter activity in INT-407 cells transiently transfected with...

...transfected with IL-8 promoter constructs deleted or mutated of a kappa B site. *V. vulnificus* infection increased the nuclear factor-kappaB (NF-kappa B) binding activity to a kappa B...

...production, NF-kappa B binding activity and I kappa B-alpha degradation induced by *V. vulnificus* infection. Taken together, these results indicate clearly that *V. vulnificus* infection significantly induces IL-8 production in human intestinal epithelial cells via NF-kappa B...

...Identifiers--NECROSI S- FACTOR- ALPHA; GENE- EXPRESSI ON; IL-8 EXPRESSI ON; CAPSULAR POLYSACCHARI DE; TRANSCI RPTI ON; AP-1; FLAGELLIN; KI NASE

19/3, K/5 (Item 2 from file: 34)

DIALOG(R) File 34: Sci Search(R) Cited Ref Sci

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02539356 Genuine Article#: LJ343 No. References: 58

Title: A CAMPYLOBACTER- JEJUNI HOMOLOG OF THE LPOD-FLBF FAMILY OF PROTEIN S

IS NECESSARY FOR FLAGELLAR BIOGENESIS

Author(s): MILLER S; PESCI EC; PICKETT CL

Corporate Source: UNI V KENTUCKY, CHANDLER MED CTR, DEPT MICROBIOL

& IMMUNOL/LEXINGTON/KY/40536; UNI V KENTUCKY, CHANDLER MED CTR, DEPT

MICROBIOL & IMMUNOL/LEXINGTON/KY/40536

Journal: INFECTION AND IMMUNITY, 1993, V61, N7 (JUL), P2930-2936

ISSN: 0019-9567

Language: ENGLISH Document Type: ARTICLE (Abstract Available)

...Abstract: the C jejuni 81-176 flbA gene was constructed. The resultant strain did not synthesize flagellin and was nonmotile.

...Identifiers--HUMAN: ANTI BODY RESPONSE; ESCHERICHIA-COLI;

CAMPYLOBACTER-CRESCENTUS; YERSINIA-PESTIS; GENES; EXPRESSI ON; INFECTI ON;

MEMBRANE; MOTILITY; SALMONELLA

Research Fronts: 91-4817 003 (LIPASE GENE; CDNA FOR STIMULATORY

GDP/GTP EXCHANGE PROTEIN; EXPRESSI ON OF MESSENGER-RNA)

91-1474 002 (FECAL BACTERIA; MICROBIAL LOOP; NONCULTURABLE VIBRIO

-VULNIFICUS CELLS; SURVIVAL OF CAMPYLOBACTERS; LAKE WATER;

POLYMERASE CHAIN-REACTION; SEASONAL PATTERNS)

91-1558 001 (RHIZOBIUM...

19/3, K/6 (Item 1 from file: 71)

DIALOG(R) File 71: ELSEVIER BIOBASE

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FLAGELLI N10585880.txt

0007698259

SUPPLIER NUMBER: 2008156797

Effect of the heat shock protein 70 on the adjuvanticity induced by a bacterial flagellin of *Vibrio vulnificus*

Shae E. L.; Soo J. B.; Soo Y. K.; Young R. K.; Joon H. R.

AUTHOR EMAIL: sel ee@honnam.ac.kr

CORRESP. AUTHOR AFFIL: Shae E. L., Research Institute of *Vibrio* Infection, Genome Research Center for Enteropathogenic Bacteria, Chonnam National University, Gwangju 501-746, South Korea

CORRESP. AUTHOR EMAIL: sel ee@honnam.ac.kr

Journal: Journal of Bacteriology and Virology (J. Bacteriol. Virol.), v35, n4, (299-305), 2005, South Korea

PUBLICATION DATE: December 1, 2005 (20051201)

CODEN: JBVOA

ISSN: 1598-2467 el ISSN: 1460-2393

RECORD TYPE: Abstract; New

DOCUMENT TYPE: Article

LANGUAGES: Korean SUMMARY LANGUAGES: English

NO. OF REFERENCES: 38

Effect of the heat shock protein 70 on the adjuvanticity induced by a bacterial flagellin of *Vibrio vulnificus*

Recently we have shown that a bacterial flagellin, *Vibrio vulnificus* FlaB (Vv-FlaB), has a strong adjuvant activity to induce protective immune response. In order to investigate the adjuvanticity of Vv-FlaB, we prepared highly purified recombinant protein

... separated Vv-FlaB and HSP70 by using a high performance protein purification chromatography and compared adjuvant activities of Vv-FlaB, HSP70 and Vv-FlaB/HSP70 mixture. Using an intranasal immunization mouse model, we observed that co-administration of the flagellin with tetanus toxoid (TT) induced significantly enhanced TT-specific antibody (Ig) responses. However contaminating doses...

... the adjuvanticity of Vv-FlaB and furthermore HSP70 alone did not enhance TT-specific Ig response and protective immunity against lethal challenge with tetanus toxin. These results show that the HSP70 contaminating Vv-FlaB...

DESCRIPTORS:

... Flagellin; ...

... *Vibrio vulnificus*

SPECIES DESCRIPTORS:

... *Vibrio*; ...

... *Vibrio vulnificus*

CLASSIFICATION DESCRIPTION:

IMMUNOLOGY AND INFECTIOUS DISEASES...

... IMMUNITY TO INFECTION

19/3, K/7 (Item 1 from file: 72)

DIALOG(R) File 72: EMBASE

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0082439768

EMBASE No: 2008273768

A bacterial flagellin, *Vibrio vulnificus* FlaB, induces

Page 26

FLAGELLI N10585880.txt

human dendritic cell maturation

Byung C.J.; Soo Y.K.; Choi B.-H.; Park M.-S.; Lee J.-J.; Joon H.R.; Shee E. L.

Department of Dental Pharmacology, School of Dentistry, Chonnam National University, Gwangju 500-757, Korea, Republic of

AUTHOR EMAIL: sel ee@honnam ac. kr

CORRESP. AUTHOR/AFFIL: Shee E. L.: Department of Dental Pharmacology, School of Dentistry, Chonnam National University, 300 Yongbong-Dong, Puk-Ku, Gwangju 500-757, Korea, Republic of

CORRESP. AUTHOR EMAIL: sel ee@honnam ac. kr

Journal of Bacteriology and Virology ( J. Bacteriol. Virol. ) (Korea, Republic of) December 1, 2005, 35/3 (209-216)

CODEN: JBVOA ISSN: 1598-2467

URL: http://210.101.116.36/EngSiteSearch/(jtiry mau0jjfgd45mf3nlpq a)/ISS

RForm.aspx#

DOCUMENT TYPE: Journal; Article RECORD TYPE: Abstract

LANGUAGE: English SUMMARY LANGUAGE: English

NUMBER OF REFERENCES: 31

A bacterial flagellin, *Vibrio vulnificus* FlaB, induces human dendritic cell maturation

The motile marine bacterium *Vibrio vulnificus* has a total of six flagellins. Flagellin is a structural component of flagellar filament in various locomotive bacteria and is the ligand...

... various types of cells including dendritic cells (DCs), recognize invading microorganisms and finally trigger host immune responses. In this study, we prepared all of six recombinant flagellin proteins and assessed the effect of six flagellins on IL-8 activation through TLR6 recognition. Although showed different activities, five out of the six flagellins stimulated significant IL-8 activation. We also investigated the immunomodulatory roles of Vv-FlaB, the crucial building block of *V. vulnificus* flagellar filament, on human dendritic cells. Treatment of immature DCs with Vv-FlaB resulted in an increased expression of co-stimulatory molecules and induced strong allo-T cell proliferative activities of the DCs. These results show that the Vv-FlaB may serve an epochal immune adjuvant possessing effective immunomodulatory activities.

DRUG DESCRIPTIONS:

\*flagellin

immunological adjuvant; interleukin 8; recombinant protein;

toll like receptor 5

MEDICAL DESCRIPTIONS:

\*cell maturation; \*dendritic cell; \*nucleotide sequence; \*Vibrio vulnificus

antigen recognition; article; cell activation; genetic transfection; human;

human cell; immune response; immunomodulation; lymphocyte

proliferation; mixed lymphocyte reaction; molecular cloning; nonhuman

CAS REGISTRY NO.: 12777-81-0 (flagellin); 114308-91-7 (interleukin 8)

19/3, K/8 (Item 1 from file: 135)

DI ALCO (R) File 135: NewsRx Weekly Reports

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0000313398 (USE FORMAT 7 OR 9 FOR FULLTEXT)

Researchers' data from Cuba, the South Korea and the United States advance vaccines research

Cancer Vaccine Week, June 26, 2006, p. 85

DOCUMENT TYPE: Expanded Reporting LANGUAGE: English

Page 27

RECORD TYPE: FULLTEXT  
WORD COUNT: 946

...TEXT: United States.

Study 1: Very small size proteoliposomes derived from *Neisseria meningitidis* are an effective adjuvant for generation of CTL responses to peptide and protein antigens.

"The development of potent adjuvants, conditioning innate and adaptive immunity, particularly CTL responses, has become currently a hot point in the rational design of vaccines for cancer immunotherapy. We have described a new approach, in which gangliosides are incorporated into vesicles from *Neisseria*...

...and F3H tumor models respectively," said Circe Mesa and colleagues at the Center of Molecular Immunology in Havana. "Also VSSP induces activation of CTL responses to co-injected trimmed peptides and...

...published their study in *Vaccine* (Very small size proteoliposomes derived from *Neisseria meningitidis*: An effective adjuvant for generation of CTL responses to peptide and protein antigens. *Vaccine*, 2006; 24(14):2692-2699).

For additional information, contact Circe Mesa, Vaccine Department, Center for Molecular Immunology, 216 Esq 15, Atabey, Playa, C Habana 16040, Cuba. circe@ct.cimsl.edu.

Study 2: A bacterial flagellin, *Vibrio vulnificus* FlA<sub>B</sub>, has a strong mucosal adjuvant activity to induce protective immunity.

"Flagellin, the structural component of flagellar filament in various locomotive bacteria, is the ligand for Toll-like receptor 5 (TLR5) of host cells. TLR stimulation by various pathogen-associated molecular patterns leads to activation of innate and subsequent adaptive immune responses. Therefore, TLR ligands are considered attractive adjuvant candidates in vaccine development. In this study, we show the highly potent mucosal adjuvant activity of a *Vibrio vulnificus* major flagellin (FlA<sub>B</sub>)," investigators in South Korea report.

"Using an intranasal immunization mouse model, we observed that co-administration of the flagellin with tetanus toxoid (TT) induced significantly enhanced TT-specific immunoglobulin A (IgA) responses in both mucosal and systemic compartments and IgG responses in the systemic...

...said Shee Eun Lee at Chonnam National University and collaborators in South Korea. "The mice immunized with TT plus FlA<sub>B</sub> were completely protected from systemic challenge with a 200x minimum lethal...

...number of TLR5-expressing cells in cervical lymph nodes."

They concluded, "These results indicate that flagellin would serve as an efficacious mucosal adjuvant inducing protective immune responses through TLR5 activation."

Lee and associates published their study in *Infection and Immunity* (A bacterial flagellin, *Vibrio vulnificus* FlA<sub>B</sub>, has a strong mucosal adjuvant activity to induce protective immunity. *Infect Immun*, 2006; 74(1):694-702).

For additional information, contact Joon Haeng Rhee, National Research Laboratory...

...Dong-Ku, Gwangju 501-746, South Korea. jhrhee@chonnam.chonnam.ac.kr.

Study 3: Active immunization with a detoxified endotoxin vaccine protects against lethal polymicrobial sepsis.

Researchers in the United States...

...core glycolipid antibody and has been tested in pilot studies in human

volunteers."

"Mice were immunized with the LPS-J5/OMP vaccine with or without synthetic oligodeoxynucleotides (ODNs) containing unmethylated CpG motifs as a vaccine adjuvant (CpG ODN). The efficacy of the vaccine-induced antibody response was tested in a cecal ligation and puncture model," said Steven M. Opal at Brown University and collaborators.

"Immunization resulted in a >20-fold increase in anti-core glycolipid antibody levels, which were further...

...puncture was performed ( $p < 0.01$ ) and significantly decreased the levels of bacteria in organs. Immunoglobulin G (IgG) anti-core glycolipid antibodies were decreased in mice to a significantly greater extent...

...sepsis."

Opal and his coauthors published their study in the Journal of Infectious Diseases (Active immunization with a detoxified endotoxin vaccine protects against lethal polymicrobial sepsis: its use with CpG adjuvant and potential mechanisms. J Infect Dis, 2005; 192(12):2074-2080).

For additional information, contact...

...Providence, Rhode Island, United States, Septicemia Vaccine, Sepsis, Septic Shock, Vaccine Development, Vaccine Efficacy, Vaccine Adjuvant, Immunology, Immunotherapy, Neisseria Meningitidis, Oligonucleotides, Proteomics.

This article was prepared by Cancer Vaccine Week editors from staff...

DESCR PTORS: Cancer Vaccine; Immunology; Immunotherapy; Neisseria Meningitidis; Oligonucleotides; On; Proteomics; Providence; Rhode Island; Sepsis; Septic Shock; Septicemia Vaccine; United States; Vaccine Adjuvant; Vaccine Development; Vaccine Efficacy; Vaccines; All News

19/3,K/9 (Item 2 from file: 135)  
DIALCQ R) File 135: NewsRx Weekly Reports  
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0000311462 (USE FORMAT 7 OR 9 FOR FULLTEXT)  
New research from Cuba, the South Korea and the United States in the area of vaccines detailed  
Cancer Vaccine Week, June 19, 2006, p.44

DOCUMENT TYPE: Expanded Reporting LANGUAGE: English  
RECORD TYPE: FULLTEXT  
WORD COUNT: 945

...TEXT: vaccines data.

Study 1: Very small size proteoliposomes derived from Neisseria meningitidis are an effective adjuvant for generation of CTL responses to peptide and protein antigens.

"The development of potent adjuvants, conditioning innate and adaptive immunity, particularly CTL responses, has become currently a hot point in the rational design of vaccines for cancer immunotherapy. We have described a new approach, in which gangliosides are incorporated into vesicles from Neisseria...

...and F3II tumor models respectively," said Circe Mesa and colleagues at the Center of Molecular Immunology in Havana. "Also VSSP induces activation of CTL responses to co-injected trimmed peptides and...

...published their study in Vaccine (Very small size proteoliposomes  
Page 29

derived from *Neisseria meningitidis*: An effective adjuvant for generation of CTL responses to peptide and protein antigens. *Vaccine*, 2006; 24(14): 2692-2699.

For additional information, contact Circe Mesa, Vaccine Department, Center for Molecular Immunology, 216 Esq 15, Atabey, Playa, C Habana 16040, Cuba. circe@ct.cimsl.edu.

Study 2: A bacterial flagellin, *Vibrio vulnificus* FlaB, has a strong mucosal adjuvant activity to induce protective immunity.

"Flagellin, the structural component of flagellar filament in various locomotive bacteria, is the ligand for Toll-like receptor 5 (TLR5) of host cells. TLR stimulation by various pathogen-associated molecular patterns leads to activation of innate and subsequent adaptive immune responses. Therefore, TLR ligands are considered attractive adjuvant candidates in vaccine development. In this study, we show the highly potent mucosal adjuvant activity of a *Vibrio vulnificus* major flagellin (FlaB)," investigators in South Korea report.

"Using an intranasal immunization mouse model, we observed that co-administration of the flagellin with tetanus toxoid (TT) induced significantly enhanced TT-specific immunoglobulin A (IgA) responses in both mucosal and systemic compartments and IgG responses in the systemic ...

... said Shae Eun Lee at Chonnam National University and collaborators in South Korea. "The mice immunized with TT plus FlaB were completely protected from systemic challenge with a 200x minimum lethal ...

... number of TLR5-expressing cells in cervical lymph nodes."

They concluded, "These results indicate that flagellin would serve as an efficacious mucosal adjuvant inducing protective immune responses through TLR5 activation."

Lee and associates published their study in *Infection and Immunity* (A bacterial flagellin, *Vibrio vulnificus* FlaB, has a strong mucosal adjuvant activity to induce protective immunity. *Infect Immun*, 2006; 74(1): 694-702).

For additional information, contact Joon Haeng Rhee, National Research Laboratory...

... Dong-Ku, Gwangju 501-746, South Korea. jhrhee@chonnam.chonnam.ac.kr.

Study 3: Active immunization with a detoxified endotoxin vaccine protects against lethal polymicrobial sepsis. Researchers in the United States...

... core glycolipid antibody and has been tested in pilot studies in human volunteers."

"Mice were immunized with the LPS-J5/QMP vaccine with or without synthetic oligodeoxynucleotides (ODNs) containing unmethylated CpG motifs as a vaccine adjuvant (CpG ODN). The efficacy of the vaccine-induced antibody response was tested in a cecal ligation and puncture model," said Steven M. Opal at Brown University and collaborators.

"Immunization resulted in a >20-fold increase in anti-core glycolipid antibody levels, which were further...

... puncture was performed ( $p < 0.01$ ) and significantly decreased the levels of bacteria in organs. Immunoglobulin G (IgG) anti-core glycolipid antibodies were decreased in mice to a significantly greater extent...

... sepsis."

Opal and his coauthors published their study in the *Journal of Infectious Diseases* (Active immunization with a detoxified endotoxin vaccine protects against lethal polymicrobial sepsis: its use with CpG adjuvant and potential mechanisms. *J Infect Dis*,

2005; 192(12):2074-2080).

For additional information, contact...

... Providence, Rhode Island, United States, Septicemia Vaccine, Sepsis, Septic Shock, Vaccine Development, Vaccine Efficacy, Vaccine Adjuvant, Immunology, Immunotherapy, Neisseria Meningitidis, Oligonucleotides, Proteomics.

This article was prepared by Cancer Vaccine Week editors from staff...

DESCRIPTORS:

Cancer Vaccine; Immunology; Immunotherapy; Neisseria Meningitidis; Oligonucleotides; On; Proteomics; Providence; Rhode Island; Sepsis; Septic Shock; Septicemia Vaccine; United States; Vaccine Adjuvant; Vaccine Development; Vaccine Efficacy; Vaccines; All News; All News

19/3,K/10 (Item 1 from file: 357)

DIALCOG(R) File 357: Derwent Biotech Res.

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0377181 DBR Accession No.: 2005-22887 PATENT

Mucosal vaccine adjuvants for preventing infectious diseases, anticancer and for contraception, comprises bacterial flagellins, as active component - bacterium flagellin and gene substitution for vaccine and disease therapy or prevention

AUTHOR: RHEE J H; LEE S E; KIM S Y

PATENT ASSIGNEE: UNIV CHONNAM NAT. 2005

PATENT NUMBER: WO 2005/0455 PATENT DATE: 20050804 WPI ACCESSION NO.:

2005-542230 (200555)

PRIORITY APPLIC. NO.: KR 1974 APPLIC. DATE: 20040112

NATIONAL APPLIC. NO.: WO 2005KR103 APPLIC. DATE: 20050112

LANGUAGE: English

... for preventing infectious diseases, anticancer and for contraception, comprises bacterial flagellins, as active component - bacterium flagellin and gene substitution for vaccine and disease therapy or prevention

... ABSTRACT: active component. DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following: (1) producing (M1) immunogen having adjuvanticity by flagellin, involves substituting the genes encoding protein antigen epitopes for the genes between the N-terminal...

... 278-377 and FlaE of amino acid sequence 276-375 among the structural components of *Vibrio vulnificus* set out in SEQ ID No. 1-12; and (2) mucosal vaccine adjuvants (II), comprising immunogens prepared by (M1), as an active component. BIOTECHNOLOGY - Preferred Adjuvant: In (I), the flagellins are originated from *V. vulnificus*, *Salmonella typhimurium*, *Listeria monocytogenes*. The flagellins are chosen from flagellin proteins of *V. vulnificus* having SEQ ID No. 2, 4, 6, 8, 10 or 12, encoded by FlaA, FlaB...

... protein or peptide vaccine. Preferred Method: In (M1), the protein antigen epitopes are tetanus toxoid, immunogenic epitopes of influenza virus, immunogenic epitopes of human papilloma virus that induces uterine cervical cancer, pneumococcal antigen PspA or sperm. ACTIVITY - Antimicrobial; Cytostatic; Contraceptive. MECHANISM OF ACTION - Vaccine. The antigen specific systemic immune response and mucosal immune adjuvanticity of the recombinant flagellin was carried out as follows. Seven-week-old Balb/c mice were intranasally immunized 3 times with phosphate

# FLAGELLIN0585880.txt

buffered saline (PBS), tetanus toxoid or with combinations of 3 of tetanus toxoid (TT) and of FlaB of *V. vulnificus* (Vv) at 7 day interval. Seven days after the last immunization, saliva, vaginal wash, and serum samples were collected to assess TT-specific systemic immune responses and mucosal immune responses. These responses were measured by enzyme linked immunosorbent assay (ELISA). The mice that were vaccinated 3 times before were observed for 7 days...

...of 200 folds of lethal doses of (TT). Results indicated that the antigen specific systemic immune response and mucosal immune response was higher in the group of TT+Vv-FlaB than that in the group of ...

DESCRIPTORS: *Vibrio vulnificus*, *Salmonella typhimurium*, *Listeria monocytogenes* flagellin, FlaA, FlaB, FlaF, FlaC, FlaD, FlaE gene substitution, human papilloma virus, influenza virus, severe-acute...

...cancer live, attenuated, killed vaccine composition, anti-sperm contraceptive vaccine, recombinant protein, peptide vaccine, ELISA, immunization in mouse, appl. infectious disease, cancer therapy, prevention bacterium papova virus orthomyxo virus SARS virus corona virus analysis immunoassay DNA sequence protein sequence (24, 37)

? DS

Set	Items	Description
S1	27	ALU- RHEE, JOON-HAENG
S2	15	RD (unique items)
S3	0	S2 AND FLAGELLIN
S4	0	S2 AND FLAG?
S5	15	S2
S6	9	ALU- LEE, SHEE-EUN
S7	5	RD (unique items)
S8	217	E1-E3
S9	0	S8 AND FLAG?
S10	0	S8 AND FLAGELLIN
S11	2	S8 AND (MUCOS? OR MUCOUS)
S12	1	RD (unique items)
S13	764	FLAGELLIN AND VIBRIO
S14	1	S13 AND TOLL(W RECEPTOR
S15	290	S13 AND (IMMUN? OR ADJUVANT OR STIMUL?)
S16	85	S15 AND (RESPONSE)
S17	41	RD (unique items)
S18	10	S17 AND VULNIFICUS
S19	10	RD (unique items)
? S	FLAGELL? AND (VULNIFICUS OR TYPHIMURIUM OR MONOCYTOGENES)	
	273044	FLAGELL?
	16828	VULNIFICUS
	270871	TYPHIMURIUM
	139539	MONOCYTOGENES
S20	9512	FLAGELL? AND (VULNIFICUS OR TYPHIMURIUM OR MONOCYTOGENES)
? S	S20 AND (IMMUN? OR ADJUVANT OR STIMUL?)	
Processing		
Processed	10 of	56 files ...
Processing		
Processed	20 of	56 files ...
Processing		
Completed processing		all files
	9512	S20
	17597612	IMMUN?
	680381	ADJUVANT
	8317022	STIMUL?
S21	3047	S20 AND (IMMUN? OR ADJUVANT OR STIMUL?)



? S S21 AND RESPONSE  
           3047 S21  
           13742212 RESPONSE  
       S22 1262 S21 AND RESPONSE  
 ? DS

Set	Items	Description
S1	27	AU= PHEE, JOON- HAENG
S2	15	RD (unique items)
S3	0	S2 AND FLAGELLIN
S4	0	S2 AND FLAG?
S5	15	S2
S6	9	AU= LEE, SHEE- EUN
S7	5	RD (unique items)
S8	217	E1- E3
S9	0	S8 AND FLAG?
S10	0	S8 AND FLAGELLIN
S11	2	S8 AND (MUCOS? OR MUCCUS)
S12	1	RD (unique items)
S13	764	FLAGELLIN AND VIBRIO
S14	1	S13 AND TOLL( W RECEPTOR
S15	290	S13 AND (IMMUN? OR ADJUVANT OR STIMUL?)
S16	85	S15 AND (RESPONSE)
S17	41	RD (unique items)
S18	10	S17 AND VULNIFICUS
S19	10	RD (unique items)
S20	9512	FLAGELL? AND (VULNIFICUS OR TYPHIMURUM OR MONOCYTOGENES)
S21	3047	S20 AND (IMMUN? OR ADJUVANT OR STIMUL?)
S22	1262	S21 AND RESPONSE
? SS	22S22 AND (MUCOS OR MUCCUS?)	
S23	1	22S22
S24	149469	MUCOS
S25	1351917	MUCOS?
S26	0	22S22 AND (MUCOS OR MUCCUS?)
? S	S22 AND (MUCOS OR MUCCUS?)	
	1262	S22
	149469	MUCOS
	1351917	MUCOS?
S27	198	S22 AND (MUCOS OR MUCCUS?)
? ED		

Ref	Items	RT	Index-term
E1	5		C9999
E2	3		C99999
E3	13906191	13	*D
E4	1		D C ORANGE NO. 17- M
E5	2		D C ORANGE 17
E6	3		D RED BLOOD CELL
E7	1		D .
E8	1		D . DENTIFER
E9	1		D . DREHERI
E10	1		D . FILISTOVA
E11	1		D . LYROI DES
E12	1		D . MICROPS AQUILONIUS

Enter P or PAGE for more

? RD

>>>Duplicate detection is not supported for File 393.

>>>Duplicate detection is not supported for File 391.

>>>Records from unsupported files will be retained in the RD set.

? DS S28 86 RD (unique items)

Set	Items	Description
S1	27	AU= FHEE, JOON-HAENG
S2	15	RD (unique items)
S3	0	S2 AND FLAGELLIN
S4	0	S2 AND FLAG?
S5	15	S2
S6	9	AU= LEE, SHEE-EUN
S7	5	RD (unique items)
S8	217	E1-E3
S9	0	S8 AND FLAG?
S10	0	S8 AND FLAGELLIN
S11	2	S8 AND (MUCOS? OR MUCCUS)
S12	1	RD (unique items)
S13	764	FLAGELLIN AND VIBRIO
S14	1	S13 AND TOLL(W RECEPTOR
S15	290	S13 AND (IMMUN? OR ADJUVANT OR STIMUL?)
S16	85	S15 AND (RESPONSE)
S17	41	RD (unique items)
S18	10	S17 AND VULNIFICUS
S19	10	RD (unique items)
S20	9512	FLAGELL? AND (VULNIFICUS OR TYPHIMURUM OR MONOCYTOGENES)
S21	3047	S20 AND (IMMUN? OR ADJUVANT OR STIMUL?)
S22	1262	S21 AND RESPONSE
S23	1	22S22
S24	149469	MUCOS
S25	1351917	MUCOS?
S26	0	22S22 AND (MUCOS OR MUCCOS?)
S27	198	S22 AND (MUCOS OR MUCCOS?)
S28	86	RD (unique items)
? S S27 AND ((TLR OR (TOLL(W RECEPTOR)) OR VACCINE)		
Processing 30 of 56 files ...		
Completed processing all files		
	198	S27
	62622	TLR
	175193	TOLL
	7738302	RECEPTOR
	2165	TOLL(W RECEPTOR
	1143005	VACCINE
S29	115	S27 AND ((TLR OR (TOLL(W RECEPTOR)) OR VACCINE)
? RD		

>>>Duplicate detection is not supported for File 393.

>>>Duplicate detection is not supported for File 391.

>>>Records from unsupported files will be retained in the RD set.

S30 47 RD (unique items)

? T S30/3, K/1-47

>>>KW C option is not available in file(s): 399

30/3, K/1 (Item 1 from file: 5)

DIALOG(R) File 5: Biosis Previews(R)

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0020983576 BIOSIS NO.: 200900325013

IgA Response of BALB/c Mice to Orally Administered Salmonella

typhimurium Flagellin-Displaying T2 Bacteriophages

AUTHOR: Synnott Aidan; Onishi Kazuhito; Nakai Yutaka; Tanji Yasunori  
(Reprint)

FLAGELLIN0585880.txt

AUTHOR ADDRESS: Tokyo Inst Technol, Dept Bi engn, M dori Ku, J2-15,  
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JOURNAL: Biotechnology Progress 25 (2, Sp. Iss. SI): p552-558 MAR-APR 2009  
2009  
ITEM IDENTIFIER: doi: 10.1021/bp.132  
ISSN: 8756-7938  
DOCUMENT TYPE: Article  
RECORD TYPE: Abstract  
LANGUAGE: English

IgA Response of BALB/c Mice to Orally Administered Salmonella  
typhimurium Flagellin-Displaying T2 Bacteriophages

ABSTRACT: Salmonella typhimurium antigens were displayed on the  
capsid of a T2 bacteriophage to explore the potential of phage display  
for an oral vaccine. Segments of the flagellin proteins FljC  
(H1 antigen) and FljB (H2) were fused to the N-terminal of T2...

...over 10 weeks and examined for phage by plaque assay and for the  
presence of mucosal IgA by, ELISA. Relatively few phages were  
detected relative to the amount administered (up to...

...at least 80-465 times lower than the protein dose administered. The  
possibility that the immunostimulatory properties of the phage  
create an adjuvant effect to enhance the immunogenic  
properties of the displayed proteins is discussed. We conclude that phage  
may be valuable as...

DESCRIPTORS:

...ORGANISMS: Salmonella typhimurium (Enterobacteriaceae...  
CHEMICALS & BIOCHEMICALS: immunoglobulin A (IgA)...

...flagellin protein, H1 antigen...

...flagellin protein, H2 antigen...

...oral vaccine; ...

...immunologic drug, immunostimulant drug, vaccine, oral  
administration...

...immunologic drug, immunostimulant drug, vaccine, oral  
administration

...METHODS & EQUIPMENT: laboratory techniques, immunologic  
techniques...

MISCELLANEOUS TERMS: immunostimulatory property

CONCEPT CODES:

30/3, K/2 (Item 2 from file: 5)  
DIALOG File 5: Biosis Previews(R)  
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0020717443 BIOSIS NO.: 200900057777

New malaria vaccine candidates based on the Plasmodium vivax  
Merozoite Surface Protein-1 and the TLR-5 agonist Salmonella  
Typhimurium FljC flagellin

AUTHOR: Bargieri Daniel Y; Rosa Daniela S; Braga Catarina J M; Carvalho  
Bruna C; Costa Fabio T M; Espindola Noeli Maria; Vaz Adelaide Jose;  
Soares Irene S; Ferreira Luis C S; Rodrigues Mauricio M (Reprint)

AUTHOR ADDRESS: Univ Fed Sao Paulo, Escola Paulista Med, CINTERGEN, Rua  
Marshall 207, BR-04044010 Sao Paulo, Brazil\*\*Brazil

AUTHOR E-MAIL ADDRESS: m.odrigues@unifesp.br  
 JOURNAL: Vaccine 26 (48): p6132-6142 NOV 11 2008 2008  
 ITEM IDENTIFIER: doi:10.1016/j.vaccine.2008.08.070  
 ISSN: 0264-410X  
 DOCUMENT TYPE: Article  
 RECORD TYPE: Abstract  
 LANGUAGE: English

New malaria vaccine candidates based on the Plasmodium vivax  
 Merozoite Surface Protein-1 and the TLR-5 agonist Salmonella  
 Typhimurium FliC flagellin

ABSTRACT: The present study evaluated the immunogenicity of new  
 malaria vaccine formulations based on the 19 kDa C-terminal  
 fragment of Plasmodium vivax Merozoite Surface Protein-1 (MSP1(19)) and  
 the Salmonella enterica serovar Typhimurium flagellin (FliC),  
 a Toll-like receptor 5 (TLR5) agonist. FHC was used as an adjuvant  
 either admixed or genetically linked to the P. vivax MSP1(19) and  
 administered to C57BL/6 mice via parenteral (s.c.) or mucosal  
 (i.n.) routes. The recombinant fusion protein preserved MSP1(19) epitopes  
 recognized by Sera collected from P. vivax infected humans and TLR5  
 agonist activity. Mice parenterally immunized with recombinant P  
 vivax MSP1 19 in the presence of FliC, either admixed or genetically...

...strong and long-lasting MSP1 (19)-specific systemic antibody responses  
 with a prevailing IgG1 subclass response. Incorporation of another  
 TLR agonist, CpG ODN 1826, resulted in a more balanced  
 response, as evaluated by the IgG1/IgG2c ratio, and higher  
 cell-mediated immune response measured by interferon-gamma  
 secretion. Finally, we show that MSP1 19-specific antibodies recognized the...

...vivax parasites harvested from infected humans. The present report  
 proposes a new class of malaria vaccine formulation based on the  
 use of malaria antigens and the innate immunity agonist FliC. It  
 contains intrinsic adjuvant properties and enhanced ability to  
 induce specific humoral and cellular immune responses when  
 administered alone or in combination with other adjuvants. (C) 2008  
 Elsevier Ltd. All...

# DESCRIPTORS:

...MAJOR CONCEPTS: Immune System  
 CHEMICALS & BIOCHEMICALS: immunoglobulin G...

...immunoglobulin G...

...Plasmodium vivax merozoite surface protein-1 vaccine-...

...immunologic-drug, immunostimulant-drug, vaccine,  
 pharmacodynamics...

...immunologic-drug, immunostimulant-drug, vaccine,  
 pharmacodynamics

MECELLANEOUS TERMS: immune response; ...

...antibody response

CONCEPT CODES:

30/3, K/3 (Item 3 from file: 5)  
 DIALOG(R) File 5: Biosis Previews(R)  
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0020367307 BIOSIS NO.: 200800414246

FLAGELLIN0585880.txt

Deferential upregulation of PD-L1 and PD-L2 expression via TLR4 and TLR5 mediated signals on colonic myofibroblasts  
AUTHOR: Planchuk Iryna V; Beswick Ellen J; Saada Jarnal I; Reyes Victor E; Powell Don W  
JOURNAL: Gastroenterology 134 (4, Suppl. 1): pA356 APR 2008 2008  
CONFERENCE/MEETING: Digestive Disease Week Meeting/109th Annual Meeting of the American Gastroenterological Association San Diego, CA, USA May 17 -22, 2008; 20080517  
SPONSOR: Amer Gastroenterol Assoc  
ISSN: 0016-5085  
DOCUMENT TYPE: Meeting; Meeting Abstract  
RECORD TYPE: Abstract  
LANGUAGE: English

... ABSTRACT: is thought to represents a disruption of tolerance to intestinal microflora, leading to dysregulation of mucosal CD4(+) T cell responses and chronic inflammation. Recent data indicate that regulation of these responses...

... it has been demonstrated that activation of CMFs (e.g., cytokine production) might occur through stimulation by pathogen-associated molecular patterns (PAMPs) via TLR signaling. Thus, we hypothesized that CMFs basal expression of PD-L1/2 molecules are among key factors in gut mucosal immune homeostasis and its expression may be altered by bacterial stimulation of toll-like receptors during IBD. Methods: PD-L1 and PDL1 expression on human CMFs in response to the bacterial stimuli in presence/absence of the inhibitors of TLR4 and TLR5 signaling was quantified using real-time RT-PCR and FACS analysis. Salmonella typhimurium was chosen as a model of bacterial PAMPs possessing well characterized TLR4 and TLR5 ligands (a.k.a. LPS and flagellin, respectively). Results: Stimulation of the CMFs with S. typhimurium for 24h resulted in a significant increase in PD-L1 and PD-L2 expression. A...

... polymixin B (10 mu g/mL). Upregulation of PD-L2 was mainly due to the stimulation of TLR5, since it was significantly decreased (50-75% by the presence of the TLR5...

... These results support our hypothesis that CMFs may engage in a suppressive effect on the response of activated CD4(+) T cells in the colonic mucosa via expression of negative PD-L1/2 co-stimulators. Our data suggest that earlier observed abnormalities in the expression of these molecules on CMFs in IBD colonic mucosa may be due to the stimulation of CMFs through TLR4 and/or TLR5 by bacterial PAMPs, of luminal origin during IBD...

#### DESCRIPTORS:

... MAJOR CONCEPTS: Immune System  
ORGANISMS: Salmonella typhimurium (Enterobacteriaceae)...  
... ORGANISMS: PARTS ETC: immune system...

... colonic mucosa -  
CHEMICALS & BIOCHEMICALS:

30/3, K/4 (Item 4 from file: 5)  
DIALOG(R) File 5: Biosis Previews(R)  
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0020189834 BIOSIS NO.: 200800236773  
A bacterial flagellin, *Vibrio vulnificus* FlaB, has a strong mucosal adjuvant activity to induce protective immunity  
AUTHOR: Lee S (Reprint); Kim S; Jeong B; Kim Y; Bae S; Choy H; Chung S;  
Page 37

Rhee J  
 AUTHOR ADDRESS: Genome Res Ctr Enteropathogen Bacteria, Res Inst Vibrio  
 Infect, Kwangju, South Korea\*\*South Korea  
 JOURNAL: Abstracts of the General Meeting of the American Society for  
 Microbiology 105 p252 2005 2005  
 CONFERENCE/MEETING: 105th General Meeting of the  
 American-Society-for-Microbiology Atlanta, GA, USA June 05 -09, 2005;  
 20050605  
 SPONSOR: Amer Soc Microbiol  
 ISSN: 1060-2011  
 DOCUMENT TYPE: Meeting; Meeting Poster  
 RECORD TYPE: Citation  
 LANGUAGE: English

A bacterial flagellin, *Vibrio vulnificus* FlaB, has a strong  
 mucosal adjuvant activity to induce protective immunity

DESCRIPTORS:

... MAJOR CONCEPTS: Immune System  
 ORGANISMS: *Vibrio vulnificus* (Vibrionaceae)  
 CHEMICALS & BIOCHEMICALS:  
 MISCELLANEOUS TERMS: immune response; ...

... vaccine development  
 CONCEPT CODES:

30/3, K/5 (Item 5 from file: 5)  
 DIALOG(R) File 5: Biosis Previews(R)  
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0020142049 BIOSIS NO.: 200800188988

A chimera of flagellin and cholera toxin as a mucosal  
 adjuvant

AUTHOR: Kim S Y (Reprint); Lee S E; Vo T D H; Bae S J; Kim K; Rhee J H  
 AUTHOR ADDRESS: Chonnam Natl Univ, Sch Med, Clin Vaccine R and D Ctr,  
 Kwangju, South Korea\*\*South Korea  
 JOURNAL: Abstracts of the General Meeting of the American Society for  
 Microbiology 107 p287 2007 2007  
 CONFERENCE/MEETING: 107th General Meeting of the  
 American-Society-for-Microbiology Toronto, CANADA 2007,  
 SPONSOR: Amer Soc Microbiol  
 ISSN: 1060-2011  
 DOCUMENT TYPE: Meeting; Meeting Abstract  
 RECORD TYPE: Citation  
 LANGUAGE: English

A chimera of flagellin and cholera toxin as a mucosal  
 adjuvant

DESCRIPTORS:

... MAJOR CONCEPTS: Immune System  
 ORGANISMS: *Vibrio vulnificus* (Vibrionaceae)  
 CHEMICALS & BIOCHEMICALS: ... flagellin; ...

... toll-like receptor 5 {TLR-5}...

... immunologic-drug, toxicity...

... immunologic-drug, toxicity  
 MISCELLANEOUS TERMS: protective immunity; ...

... systemic immune response; ...

... immunogenicity; ...

...mucosal immune response; ...

...mucosal adjuvant activity  
CONCEPT CODES:

30/3,K/6 (Item 6 from file: 5)  
DIALOG(R) File 5: Biosis Previews(R)  
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0020061095 BIOSIS NO.: 200800108034  
Mucosal delivery of a transmission-blocking DNA vaccine  
encoding *Gardia lamblia* CWP2 by *Salmonella typhimurium*  
bactofection vehicle  
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JOURNAL: Vaccine 25 (50): p8372-8383 DEC 5 2007 2007  
ITEM IDENTIFIER: doi:10.1016/j.vaccine.2007.10.012  
ISSN: 0264-410X  
DOCUMENT TYPE: Article  
RECORD TYPE: Abstract  
LANGUAGE: English

Mucosal delivery of a transmission-blocking DNA vaccine  
encoding *Gardia lamblia* CWP2 by *Salmonella typhimurium*  
bactofection vehicle

ABSTRACT: In this study, we investigated the use of *Salmonella typhimurium* (STMI strain) as a bactofection vehicle to deliver a transmission-blocking DNA vaccine (TBDV) plasmid to the intestinal immune system. The gene encoding the full length cyst wall protein-2 (CWP2) from *Gardia lamblia* was subcloned into the pCDNA3 mammalian expression vector and stably introduced into *S. typhimurium* STMI. Eight-week-old female BALB/c mice were orally immunized every 2 weeks, for a total of three immunizations. Vaccinated and control mice were sacrificed 1 week following the last injection. Administration of the DNA vaccine led to the production of CWP2-specific cellular immune responses characterized by a mixed Th1/Th2 response. Using ELISA, antigen-specific IgA and IgG antibodies were detected in intestinal secretions. Moreover, analysis of sera demonstrated that the DNA immunization also stimulated the production of CWP2-specific IgG antibodies that were mainly of the IgG2a isotype. Finally, challenge infection with live *Gardia muris* cysts revealed that mice receiving the CWP2-encoding DNA vaccine were able to reduce cyst shedding by similar to 60% compared to control mice. These results demonstrate, for the first time, the development of parasite transmission-blocking immunity at the intestinal level following the administration of a mucosal DNA vaccine delivered by *S. typhimurium* STMI. (c) 2007 Elsevier Ltd. All rights reserved.

DESCRIPTORS:  
...MAJOR CONCEPTS: Immune System  
...BIOSYSTEMATIC NAMES: Flagellata--  
ORGANISMS: *Salmonella typhimurium* (Enterobacteriaceae, ...

...*Gardia lamblia* (Flagellata); ...

...*Gardia muris* (Flagellata)--  
CHEMICALS & BIOCHEMICALS: immunoglobulin A...

...immunoglobulin G...

...transmission-blocking DNA vaccine-...

...immunologic-drug, immunostimulant-drug

BIOSYSTEMATIC CODES:

...35200 Flagellata

COMMON TAXONOMIC TERMS:

30/3, K/7 (Item 7 from file: 5)  
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0019584323 BIOSIS NO.: 200700244064

Flagellin-induced tolerance of the Toll-like receptor 5 signaling pathway in polarized intestinal epithelial cells

AUTHOR: Sun Jun (Reprint); Fegan Pamela E; Desai Anjali S; Madara James L; Hobert Michael E

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JOURNAL: American Journal of Physiology - Gastrointestinal and Liver Physiology 292 (3): pG767-G778 MAR 2007 2007

ISSN: 0193-1857

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: English

Flagellin-induced tolerance of the Toll-like receptor 5 signaling pathway in polarized intestinal epithelial cells

ABSTRACT: Salmonella typhimurium is a gram-negative enteric pathogen that invades the mucosal epithelium and is associated with diarrheal illness in humans. Flagellin from S. typhimurium and other gram-negative bacteria has been shown to be the predominant proinflammatory mediator through...

...basolateral Toll-like receptor 5 (TLR5). Recent evidence has shown that prior exposure can render immune cells tolerant to subsequent challenges by TLR ligands. Accordingly, we examined whether prior exposure to purified flagellin would render human intestinal epithelial cells insensitive to future contact. We found that flagellin-induced tolerance is common to polarized epithelial cells and prevents further activation of proinflammatory signaling cascades by both purified flagellin and Salmonella bacteria but does not affect TNF- $\alpha$  stimulation of the same pathways. Flagellin tolerance is a rapid process that does not require protein synthesis, and that occurs within 1 to 2 h of flagellin exposure. Prolonged flagellin exposure blocks activation of the NF- $\kappa$ B, MAPK, and phosphoinositol 3-kinase signaling pathways...

...the basolateral TLR5 without affecting the polarity or total expression of TLR5. After removal of flagellin, cells require more than 24 h to fully recover their ability to mount a normal proinflammatory response. We have found that activation of phosphoinositol 3-kinase and Akt by flagellin has a small dampening effect in the early stages of flagellin signaling but is not responsible for tolerance. Our study indicates that inhibition of TLR5-associated IL-1 receptor-associated kinase-4 activity occurs during the development of flagellin tolerance and is likely to be the cause of tolerance.



DESCRIPTORS:

... ORGANISM: *Salmonella typhimurium* (Enterobacteriaceae)...  
CHEMICALS & BIOCHEMICALS: ...flagellin;

30/3, K/8 (Item 8 from file: 5)  
DIALOG File 5: Biosis Previews(R)  
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19369902 BIOSIS NO.: 200700029643

Genetically engineered *Bifidobacterium animalis* expressing the *Salmonella* flagellin gene for the mucosal immunization in a mouse model

AUTHOR: Takata Tetsuo; Shirakawa Toshiro (Reprint); Kawasaki Yoshiko; Kinoshita Shohiro; Gotoh Akinobu; Kano Yasunobu; Kawabata Masato  
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JOURNAL: JOURNAL OF GENE MEDICINE 8 (11): p1341-1346 NOV 2006 2006  
ISSN: 1099-498X(print) 1521-2254\_(electronic)  
DOCUMENT TYPE: Article  
RECORD TYPE: Abstract  
LANGUAGE: English

Genetically engineered *Bifidobacterium animalis* expressing the *Salmonella* flagellin gene for the mucosal immunization in a mouse model

**ABSTRACT:** Background A critical component of the host defense against enteric infections is the immunological response of the mucosal membrane, a major starting point of infectious disease, such as typhoid fever. The mucosal immune system consists of an integrated network of lymphoid tissues, mucous membrane-associated cells, and effector molecules. In the present study, we developed a recombinant *Bifidobacterium animalis* (*B. animalis*) genetically modified with the *Salmonella* flagellin gene for mucosal immunization as an oral typhoid vaccine. **Methods** We constructed an oral vaccine against *Salmonella typhimurium*, consisting of recombinant *B. animalis* containing the flagellin gene of *Salmonella*. The recombinant *B. animalis* was administered orally to mice every other day for 6 weeks. Anti-flagellin antibodies in the serum and stools were measured by enzyme-linked immunosorbent assay (ELISA). **Results** We detected significantly higher levels of flagellin-specific IgA in the serum and stools of the mice treated with the recombinant *B. animalis* containing the flagellin gene than was seen in those treated with parental *B. animalis*. **Conclusions** Our findings suggest that an oral vaccination using recombinant *B. animalis* genetically modified with the flagellin gene of *Salmonella* may be effective against *Salmonella* infections. Copyright (c) 2006 John Wiley & Sons...

DESCRIPTORS:

... MAJOR CONCEPTS: Immune System  
... ORGANISM: *Salmonella typhimurium* (Enterobacteriaceae)...  
DISEASES: *Salmonella typhimurium* infection...  
CHEMICALS & BIOCHEMICALS: typhoid vaccine-....

... immunologic-drug, immunostimulant-drug, vaccine, oral administration  
GENE NAME: *Salmonella* flagellin gene (Enterobacteriaceae)  
... METHODS & EQUIPMENT: mucosal immunization-

30/3, K/9 (Item 9 from file: 5)  
 DIALOG(R) File 5: Biosis Previews(R)  
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19277223 BIOSIS NO.: 200600622618  
 Flagellin suppresses epithelial apoptosis and limits disease during enteric infection  
 AUTHOR: Vijay-Kumar Matam; Wu Hui-xia; Jones Rheinalt; Grant George; Babbini Brian; King Timothy P; Kelly Denise; Gewirtz Andrew T; Neish Andrew S (Reprint)  
 AUTHOR ADDRESS: Emory Univ, Sch Med, Dept Pathol, Room 105F, Whitehead Bldg, 615 Michael St., Atlanta, GA 30322 USA\*\*USA  
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 JOURNAL: American Journal of Pathology 169 (5): p1686-1700 NOV 2006 2006  
 ISSN: 0002-9440  
 DOCUMENT TYPE: Article  
 RECORD TYPE: Abstract  
 LANGUAGE: English

Flagellin suppresses epithelial apoptosis and limits disease during enteric infection

ABSTRACT: Flagellin, the primary component of bacterial flagella, is a potent activator of toll-like receptor 5 (TLR5) signaling and is a major...  
 ...effector molecules in murine models of salmonellosis and that these mutants elicit markedly reduced early mucosal inflammation relative to their isogenic parent strains. Conversely, flagellate bacteria were more potent activators of epithelial caspases and subsequent apoptosis. These phenomena correlated with a delayed but markedly exacerbated mucosal inflammation at the later stages of infection as well as elevated extraintestinal and systemic bacterial load, culminating in a more severe clinical outcome. Systemic administration of exogenous flagellin primarily reversed the deleterious effects of in vivo Salmonella infection. These observations indicate that in Salmonella infection, flagellin plays a dominant role in activation of not only innate immunity but also anti-apoptotic processes in epithelial cells. These latter TLR-mediated responses that delay epithelial apoptosis may be as critical to mucosal defense as the classic acute inflammatory response. This notion is consistent with the emerging paradigm that specific TLR ligands may have a fundamental cytoprotective effect during inflammatory stress.

#### DESCRIPTORS:

... MAJOR CONCEPTS: Immune System  
 ... ORGANIC SMS: pathogen, serovar-typhimurium strain-SL3201...  
 ORGANIC SMS: PARTS ETC: flagella  
 DISEASES: mucosal inflammation...

... immune system disease  
 CHEMICALS & BIOCHEMICALS: flagellin;

30/3, K/10 (Item 10 from file: 5)  
 DIALOG(R) File 5: Biosis Previews(R)  
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19275867 BIOSIS NO.: 200600621262  
 Safety and immunogenicity of attenuated Salmonella enterica serovar Typhimurium delivering an HIV-1 Gag antigen via the Salmonella Type III secretion system  
 AUTHOR: Kotton Camille N; Lankowski Alexander J; Scott Nathaniel; Sisul David; Chen Li Mei; Raschke Katherine; Borders Genevieve; Boaz Mark;  
 Page 42

FLAGELLI N10585880.txt

Spentzou Aggeliki; Galan Jorge E; Hohmann Elizabeth L (Reprint)  
AUTHOR ADDRESS: Harvard Univ, Sch Med, Massachusetts Gen Hosp, Infect Dis  
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JOURNAL: Vaccine 24 (37-39): p6216-6224 SEP 11 2006 2006  
ISSN: 0264-410X  
DOCUMENT TYPE: Article  
RECORD TYPE: Abstract  
LANGUAGE: English

Safety and immunogenicity of attenuated *Salmonella enterica* serovar  
Typhimurium delivering an HIV-1 Gag antigen via the *Salmonella* Type  
III secretion system

ABSTRACT: Background: CKS257 (*Salmonella typhimurium* SL1344 Delta  
phoP/phoQ Delta aroA Delta asd Delta strA/strB pSB2131) is a live oral  
vaccine vector expressing HIV Gag. Methods: HIV Gag was expressed as  
a fusion protein of a...

...1 x 10(10) CFU of CKS257 and were monitored for clinical events,  
shedding and immune responses. Results: Adverse events were mild  
except at the highest dose. Volunteers shed the organism...  
...1 days (range 0-13 days). Eighty-three percent (15/18) of subjects had a  
mucosal immune response to *Salmonella* LPS and  
flagella by IgA ELISPOT assay. Seventy-two percent (13/18) of  
subjects seroconverted to *Salmonella* antigens. No volunteer had a  
response to recombinant Gag as measured by serology, IgA ELISPOT,  
or immediate ex vivo gamma-interferon ELISPOT response to Gag  
peptide pools. Two volunteers responded to Gag peptides by IL-2 ELISPOT,  
and 4 of 10 volunteers receiving  $\geq 5 \times 10(8)$  CFU had a response to  
HIV peptides in a cultured gamma-interferon ELISPOT assay. Conclusions:  
Although immunogenicity of the HIV antigen needs augmentation, the  
attenuated *Salmonella* strain proved to be an excellent platform for  
vaccine development. (c) 2006 Elsevier Ltd. All rights reserved.

#### DESCRIPTORS:

... MAJOR CONCEPTS: Immune System  
... ORGANISMS: pathogen, serovar- Typhimurium strain-SL1344...  
... HIV-1 {Human immunodeficiency virus 1} (Retroviridae)...  
DI SEASES: human immunodeficiency virus infection...  
... viral disease, infectious disease, immune system disease,  
prevention and control, genetics  
CHEMICALS & BIOCHEMICALS: ... IgA {immunoglobulin A}...  
... immunologic-drug, immunostimulant-drug  
GENE NAME: *Salmonella typhimurium* asd gene (Enterobacteriaceae) {  
*Salmonella typhimurium* aspartate-semialdehyde dehydrogenase gene  
...  
... *Salmonella typhimurium* aroA gene (Enterobacteriaceae) {*Salmonella*  
*typhimurium* 3-phosphoshikimate 1-carboxyvinyltransferase gene...  
... *Salmonella typhimurium* strA gene (Enterobacteriaceae) {*Salmonella*  
*typhimurium* streptomycin resistance protein A gene...  
... *Salmonella typhimurium* strB gene (Enterobacteriaceae) {*Salmonella*  
*typhimurium* streptomycin resistance protein B gene...  
... *Salmonella typhimurium* phoP gene (Enterobacteriaceae) {*Salmonella*  
*typhimurium* response regulator gene...}

FLAGELLI N10585880.txt

... Salmonella typhimurium phoQ gene (Enterobacteriaceae) {Salmonella  
typhimurium sensor kinase protein gene}  
M SOELLANEUS TERMS: immunogenicity  
CONCEPT CODES:

30/3, K/11 (Item 11 from file: 5)  
DI ALCOFF File 5: Biosis Previews(R)  
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17967653 BIOSIS NO.: 200400338442  
Host and bacterial factors affecting induction of immune responses to  
flagellin expressed by attenuated Salmonella vaccine strains  
AUTHOR: Sbragi o-Almeida M E; Mosca T; Massis L A; Abrahamsohn I A; Ferreira  
L C S (Reprint)  
AUTHOR ADDRESS: Dept Microbiol Inst Ciencias Biomed, Univ Sao Paulo, Av Prof  
Lineu Prestes 1374, BR-05508900, Sao Paulo, Brazil\*\*Brazil  
AUTHOR E-MAIL ADDRESS: lcsf@sp.br  
JOURNAL: Infection and Immunity 72 (5): p2546-2555 May 2004 2004  
MEDIUM print  
ISSN: 0019-9567 (ISSN print)  
DOCUMENT TYPE: Article  
RECORD TYPE: Abstract  
LANGUAGE: English

Host and bacterial factors affecting induction of immune responses to  
flagellin expressed by attenuated Salmonella vaccine strains

... ABSTRACT: observations demonstrated that the delivery of recombinant  
Salmonella enterica serovar Dublin strains to mice via mucosal  
routes did not efficiently activate systemic and secreted antibody  
responses to either type d flagellin or genetically fused  
heterologous B-cell epitopes, thus reducing the usefulness of the protein  
as a carrier of epitopes for vaccine purposes. In this work, we  
investigated murine systemic and mucosal flagellin  
immunogenicity after oral immunization with attenuated  
Salmonella strains. The reduced anti-type d flagellin antibody  
responses in mice immunized via mucosal routes with three  
doses of flagellated S. enterica serovar Dublin strains were not  
caused by oral tolerance and could not be restored by coadministration of  
a mucosal adjuvant. The induction of antibody responses to  
Salmonella flagellins was shown to differ according to the genetic  
background, but not the haplotype, of the mouse lineage. Moreover, BALB/c  
mice orally immunized with S. enterica serovar Typhimurium  
strains developed anti-type i flagellin sera and secreted antibody  
responses, which indicated that the serovar of the Salmonella  
vaccine strain also affected flagellin immunogenicity.  
Analyses of cytokine responses of BALB/c mice immunized with three  
oral doses of flagellated S. enterica serovar Dublin vaccine  
strains showed that, in spite of the lack of antibody responses, elevated  
type d flagellin-specific CD4-cell-activation-dependent gamma  
interferon (IFN-gamma) and interleukin-10 responses were elicited after  
the administration of the vaccine strains via either parenteral or  
mucosal routes. Similar cytokine production patterns were detected  
to a T-cell heterologous epitope, derived from the CFA/I fimbriae of  
enterotoxigenic Escherichia coli (ETEC), in mice orally immunized  
with a Salmonella vaccine strain expressing hybrid flagella.  
These results indicate that the immunogenicities of Salmonella  
flagellins can differ significantly, depending on the murine host  
and on the bacterial vector used, and demonstrate that the induction of  
CD4-cell-activation-dependent IFN-gamma production represents a major  
immune response triggered by flagellin and in-frame  
fused heterologous T-cell epitopes after the oral administration of

FLAGELLI N10585880.txt  
recombinant *S. enterica* serovar Dublin vaccine strains.

DESCRIPTORS:

MAJOR CONCEPTS: Immune System...  
...ORGANISMS: attenuated vaccine strains, immune  
response, oral immunization, serovar-Dublin...  
CHEMICALS & BIOCHEMICALS: flagellin-...

...attenuated *Salmonella* vaccine strain expression, bacterial factor  
effects, host factor effects, immune response  
...METHODS & EQUIPMENT: immunologic techniques, laboratory  
techniques

30/3, K/12 (Item 12 from file: 5)  
DIAGNOSTIC File 5: Biosis Previews(R)  
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17661378 BIOSIS NO.: 200400032135  
HELI COBACTER PYLORI EVADES TOLL-LIKE RECEPTOR 5 INNATE IMMUNITY.  
AUTHOR: Gewirtz Andrew (Reprint); Krishna Uma; Israel Dawn; Yu Yimin; Peek  
Richard M  
AUTHOR ADDRESS: Atlanta, GA, USA\*\*USA  
JOURNAL: Digestive Disease Week Abstracts and Itinerary Planner 2003 p  
Abstract No. V007 2003 2003  
MEDIUM: e-file  
CONFERENCE/MEETING: Digestive Disease 2003 FL, Orlando, USA May 17-22,  
2003; 20030517  
SPONSOR: American Association for the Study of Liver Diseases  
American Gastroenterological Association  
American Society for Gastrointestinal Endoscopy  
Society for Surgery of the Alimentary Tract  
DOCUMENT TYPE: Meeting; Meeting Abstract; Meeting Poster  
RECORD TYPE: Abstract  
LANGUAGE: English

HELI COBACTER PYLORI EVADES TOLL-LIKE RECEPTOR 5 INNATE IMMUNITY.

...ABSTRACT: Toll-like receptor 4 (TLR4)-mediated signaling, thereby  
facilitating evasion of this mode of innate immunity. Epithelial  
surface-expressed TLR5 can be activated by flagellins expressed by  
Gram-negative mucosal bacteria, such as *S. typhimurium* and *E. coli*,  
and this results in IL-8 secretion. Since *H. pylori* is a  
flagellated pathogen, we asked whether TLR5-mediated innate  
immunity was functional in gastric epithelium and if so, does *H. pylori*  
activate or evade this...

...Thus, the goal of this study was to investigate the capacity of FlAa,  
the primary flagellar structural component of *H. pylori*, to induce  
IL-8 in gastric epithelial cells. Methods: AGS...

...with wild-type *H. pylori* strain 60190 or an isogenic flAa- mutant, or  
purified *S. typhimurium* flagellin. *H. pylori* FlAa was  
detected by Western blot using a polyclonal antiserum raised against *E. coli*  
flagellin. IL-8 was quantified in co-culture supernatants by  
ELISA. Results: *H. pylori* FlAa exhibited significant homology at the  
amino acid level to *S. typhimurium* flagellin, and was  
detected in *H. pylori* whole cell preparations and sonicates. In contrast  
to *S. typhimurium*, however, flagellin was not detected in *H. pylori*  
supernatants, even when concentrated. IL-8 levels were  
significantly ( $p < 0.001$ ) increased in AGS cells following treatment with  
*S. typhimurium* flagellin (mean  $\pm$  SD; 2,471  $\pm$  56 vs. 56  
 $\pm$  17 pg/ml; flagellin vs. control, respectively), indicating that

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TLR5 is expressed and functional in this gastric cell line. However, FlAa-containing *H. pylori* sonicates failed to activate this response. Furthermore, isogenic inactivation of *H. pylori* flAa abolished FlAa expression and resulted in decreased motility...

...*H. pylori* to induce IL-8 from AGS cells. Conclusions: Although *H. pylori* expresses a flagellin (FlAa) that is highly homologous to flagellins expressed by other Gram-negative bacteria, it does not activate TLR5-dependent IL-8 secretion...

...cells. These findings suggest that, in contrast to epithelial cell-driven inflammatory responses to *S. typhimurium* flagellin that eventuate in rapid clearance of the pathogen, *H. pylori* possesses a non-inflammatory flagellin, which may contribute to the ability of this bacterial species to persist for the virtual...

DESCRIPTORS:

...MAJOR CONCEPTS: Immune System

...ORGANISMS: *Salmonella typhimurium*

(Enterobacteriaceae...

CHEMICALS & BIOCHEMICALS: ...flagellin; ...

...toll-like receptor 5 (TLR-5)

...SCIENTIFIC TERMS: innate immunity;

CONCEPT CODES:

30/3, K/13 (Item 13 from file: 5)

DIALOG(R) File 5: Biosis Previews(R)

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17101350 BIOSIS NO.: 200300060069

Development of a mucosal complex vaccine against oral

*Salmonella* infection in mice.

AUTHOR: Harada Hiroko; Nishikawa Fumiko; Hgashi Nobutaka; Kita Eiji  
(Reprint)

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JOURNAL: Microbiology and Immunology 46 (12): p891-905 2002 2002

MEDIUM: print

ISSN: 0385-5600 (ISSN print)

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: English

Development of a mucosal complex vaccine against oral

*Salmonella* infection in mice.

ABSTRACT: We examined the immunogenicity of a *Salmonella enterica* complex vaccine (CV), consisting of flagellin and polysome purified from serotype Typhimurium LT2. CV plus cholera toxin (CT), in three oral doses given at 7-day intervals...

...on C57BL/6 mice against lethal oral infection with a wild-type strain. It elicited mucosal IgA>IgG2a>IgG1 and systemic IgG2a>IgG1>IgA antibodies to flagellin and polysome, and delayed footpad response (DFR) to both antigens. In Peyer's patches (PPs) and lamina propria (LP), IgA was...

...CD4+T cells from produced interleukin (IL)-2, interferon (IFN)-gamma, and IL-10 by stimulation with salmonella extract. On the same protocol, flagellin plus CT induced flagellin-specific

FLAGELLI N10585880.txt

mucosal and systemic IgA and IgG1 antibodies, CD4+T cells producing IL-10 and IFN-gamma in PPs and LP, and only minimal levels of flagellin-specific DFR. Polysome plus CT induced polysome-specific mucosal and systemic IgG2a in addition to IgG1 and IgA antibodies, CD4+T cells producing IFN...

...at most 50-60% survival rates. Our results suggest that polysomes in CV provide effective adjuvant activity for the induction of both mucosal and systemic Th1-biased responses toward flagellin.

#### DESCRIPTIONS:

... MAJOR CONCEPTS: Immune System

... ORGANISMS: pathogen, serovar-typhimurium LT2...

... ORGANISMS: PARTS ETC: immune system

CHEMICALS & BIOCHEMICALS: Salmonella enterica complex vaccine-

...

... immunogenicity; ...

... IgG-1 {immunoglobulin G-1...}

... IgG-2a {immunoglobulin G-2a...}

... IgA {immunoglobulin A}

MISCELLANEOUS TERMS: delayed footpad response

CONCEPT CODES:

30/3, K/14 (Item 14 from file: 5)

DIALOG File 5: Biosis Previews(R)

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16902147 BIOSIS NO.: 200200495658

Cruzipain induces both mucosal and systemic protection against

Trypanosoma cruzi in mice

AUTHOR: Schnapp Anita R; Eickhoff Chris S; Sizemore Donata; Qurtiss Roy III; Hoft Daniel F (Reprint)

AUTHOR ADDRESS: Division of Infectious Diseases and Immunology, St. Louis University Health Sciences Center, Saint Louis, MO, 63110, USA\*\*USA

JOURNAL: Infection and Immunity 70 (9): p5065-5074 September, 2002 2002

MEDIUM: print

ISSN: 0019-9567

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: English

Cruzipain induces both mucosal and systemic protection against

Trypanosoma cruzi in mice

... ABSTRACT: of Trypanosoma cruzi, is expressed by all developmental forms and strains of the parasite and stimulates potent humoral and cellular immune responses during infection in both humans and mice. This information suggested that cruzipain could be used to develop an effective T. cruzi vaccine. To study whether cruzipain-specific T cells could inhibit T. cruzi intracellular replication, we generated...

... protective effects in vivo of cruzipain-specific Th1 responses against systemic T. cruzi challenges, we immunized mice with recombinant cruzipain plus interleukin 12 (IL-12) and a neutralizing anti-IL-4 mAb. These immunized mice developed potent cruzipain-specific memory Th1 cell responses and were significantly protected against normally...

... systemic T. cruzi challenges. Although cruzipain-specific Th1 responses

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were associated with *T. cruzi* protective immunity in vitro and in vivo, adoptive transfer of cruzipain-specific Th1 cells alone did not protect BALB/c histocompatible mice, indicating that additional immune mechanisms are important for cruzipain-specific immunity. To study whether cruzipain could induce mucosal immune responses relevant for vaccine development, we prepared recombinant attenuated *Salmonella enterica* serovar Typhimurium vaccines expressing cruzipain. BALB/c mice immunized with *Salmonella* expressing cruzipain were significantly protected against *T. cruzi* mucosal infection. Overall, these data indicate that cruzipain is an important *T. cruzi* vaccine candidate and that protective *T. cruzi* vaccines will need to induce more than CD4+ Th1...

DESCRIPTORS:

MAJOR CONCEPTS: Immune System..

BIOSYSTEMATIC NAMES: Flagellata--

ORGANISMS: Trypanosoma cruzi (Flagellata)--...

...immune response, parasite

CHEMICALS & BIOCHEMICALS: ...Trypanosoma cruzi mucosal protection induction, Trypanosoma cruzi systemic protection induction, mouse immunization, vaccine candidate

BIOSYSTEMATIC CODES:

35200 Flagellata

COMMON TAXONOMIC TERMS:

30/3, K/15 (Item 15 from file: 5)

DIALOG R File 5: Biosis Previews(R)

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14124326 BIOSIS NO.: 199799758386

Systemic and local antibody response in mice induced by a recombinant peptide fragment from *Giardia lamblia* variant surface protein (VSP) H7 produced by a *Salmonella typhimurium* vaccine strain

AUTHOR: Stager S; Gottstein B; Muller N (Reprint)

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JOURNAL: International Journal for Parasitology 27 (8): p965-971 1997 1997

ISSN: 0020-7519

DOCUMENT TYPE: Article

RECORD TYPE: Abstract

LANGUAGE: English

Systemic and local antibody response in mice induced by a recombinant peptide fragment from *Giardia lamblia* variant surface protein (VSP) H7 produced by a *Salmonella typhimurium* vaccine strain

...ABSTRACT: characterized *G. lamblia* clone GS/M83-H7 was expressed in the live-attenuated *Salmonella typhimurium* vaccine strain LT2MIC. The recombinant vaccine was assessed for its potential to induce both a systemic and a local antibody response in mice. Peroral administration of the vaccine stimulated synthesis of serum IgG and intestinal IgA antibodies directed against *Salmonella* antigens as well as...

...in vaccinated animals. Taken together, these data indicate a strong intrinsic antigenicity of VSPH7, which stimulates a T-Helper2-cell pathway of the murine immune system independent of the route of antigen administration. Furthermore, the high immunostimulatory potential of the recombinant *Salmonella*/VSPH7 model vaccine



FLAGELLI N10585880.txt  
suggests application of LT2M/C as an enteric biocarrier for the  
identification of putative new target...

DESCRIPTORS:

MAJOR CONCEPTS: Immune System...  
...BIOSYSTEMATIC NAMES: Flagellata-  
ORGANISMS: Salmonella typhimurium (Enterobacteriaceae)...

...Giardia lamblia (Flagellata);  
CHEMICALS & BIOCHEMICALS:  
MISCELLANEOUS TERMS: ANTIBODY RESPONSE; ...

...IMMUNE SYSTEM...

...IMMUNOGLOBULIN A...

...IMMUNOGLOBULIN G...

...MUCOSAL IMMUNE RESPONSE; ...

...TARGET VACCINE;  
CONCEPT CODES:  
BIOSYSTEMATIC CODES:  
...35200 Flagellata

COMMON TAXONOMIC TERMS:

30/3, K/16 (Item 16 from file: 5)  
DIALOG File 5: Biosis Previews(R)  
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12624948 BIOSIS NO.: 199598092781  
Systemic and mucosal intestinal antibody response of sheep  
immunized with aromatic-dependent live or killed Salmonella  
typhimurium  
AUTHOR: Mukkur T K S (Reprint); Walker K H; Baker P; Jones D  
AUTHOR ADDRESS: CSIRO Div. Anim. Health, McMaster Lab., Private Bag No. 1,  
Gebe, NSW 2037, Australia\*\*Australia  
JOURNAL: Comparative Immunology Microbiology and Infectious Diseases 18 (1  
): p27-39 1995 1995  
ISSN: 0147-9571  
DOCUMENT TYPE: Article  
RECORD TYPE: Abstract  
LANGUAGE: English

Systemic and mucosal intestinal antibody response of sheep  
immunized with aromatic-dependent live or killed Salmonella  
typhimurium

...ABSTRACT: suitable formulation capable of inhibiting intestinal  
proteolytic activity, the total anti-lipopolysaccharide (LPS) and anti-  
flagellin (Fla) antibody response and isotype in the sera and  
intestinal washings of sheep, immunized with live  
aromatic-dependent (aro) Salmonella typhimurium strain CS332 by the  
intramuscular (live i.m.) or oral (live oral) route or acetone-killed  
virulent S. typhimurium by the intramuscular route (killed i.m.),  
were determined at various intervals post-immunization. The serum  
or intestinal anti-lipopolysaccharide (LPS) or anti-flagellin (Fla)  
antibody titres of immunized sheep, regardless of the route of  
immunization, were significantly greater (P < 0.01) than those of  
non-immune control sheep. Although significant differences between  
the serum anti-LPS or anti-Fla antibody titres of sheep in various

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immunization regimes were observed, they were not consistent for different periods post-immunization. The predominant isotype contributing to serum anti-LPS antibody activity was IgM whereas the serum...

...contribution of the IgA antibody isotype was minimal. Antibody activity in the intestinal washings of immunized sheep, regardless of the route of immunization was significantly greater ( $P < 0.01$ ) than that in non-immune control sheep. However, the titres in sheep immunized with the live *S. typhimurium* vaccines were significantly greater than those immunized with the killed vaccine. The major anti-LPS or anti-flagellin antibody isotype in the intestinal washings of sheep in the live i.m. or live oral groups was IgM at day 7 post-immunization followed by IgG1 and IgG2 at days 14 and 21 post-immunization, with only a minimal contribution by the IgA antibody isotype. On the other hand, the major antibody isotype in the intestinal washings of sheep immunized with the killed *S. typhimurium* was IgG1.

DESCRIPTIONS:

... MAJOR CONCEPTS: Immune System

... ORGANISMS: *Salmonella typhimurium* (Enterobacteriaceae)

CHEMICALS & BIOCHEMICALS:

MISCELLANEOUS TERMS: IMMUNITY

CONCEPT CODES:

30/3, K/17 (Item 1 from file: 24)

DIALOG(R) File 24: CSA Life Sciences Abstracts

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0003179679 IP ACCESSION NO: 8028984

Genetically engineered *Bifidobacterium animalis* expressing the *Salmonella* flagellin gene for the mucosal immunization in a mouse model

Takata, Tetsuo; Shirakawa, Toshiro; Kawasaki, Yoshioko; Kinoshita, Shohiro; Gotoh, Akinobu; Kano, Yasunobu; Kawabata, Masato  
International Center for Medical Research and Treatment, Kobe University  
School of Medicine, Kobe 650-0017, Japan, [mailto:toshiro@med.kobe-u.ac.jp]

Journal of Gene Medicine, v 8, n 11, p 1341-1346, November 2006

PUBLICATION DATE: 2006

PUBLISHER: John Wiley & Sons, Baffins Lane Chichester W Sussex PO19 1UD  
UK, [mailto:customer@wiley.co.uk], [URL: <http://www.wiley.com/>]

DOCUMENT TYPE: Journal Article

RECORD TYPE: Abstract

LANGUAGE: English

SUMMARY LANGUAGE: English

ISSN: 1099-498X

ELECTRONIC ISSN: 1521-2254

FILE SEGMENT: Biotechnology Research Abstracts

Genetically engineered *Bifidobacterium animalis* expressing the *Salmonella* flagellin gene for the mucosal immunization in a mouse model

ABSTRACT:

Background A critical component of the host defense against enteric infections is the immunological response of the mucosal membrane, a major starting point of infectious disease, such as typhoid

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fever. The mucosal immune system consists of an integrated network of lymphoid tissues, mucous membrane-associated cells, and effector molecules. In the present study, we developed a recombinant *Bifidobacterium animalis* (*B. animalis*) genetically modified with the *Salmonella* flagellin gene for mucosal immunization as an oral typhoid vaccine. Methods We constructed an oral vaccine against *Salmonella typhimurium* consisting of recombinant *B. animalis* containing the flagellin gene of *Salmonella*. The recombinant *B. animalis* was administered orally to mice every other day for 6 weeks. Anti-flagellin antibodies in the serum and stools were measured by enzyme-linked immunosorbent assay (ELISA). Results We detected significantly higher levels of flagellin-specific IgA in the serum and stools of the mice treated with the recombinant *B. animalis* containing the flagellin gene than was seen in those treated with parental *B. animalis*. Conclusions Our findings suggest that an oral vaccination using recombinant *B. animalis* genetically modified with the flagellin gene of *Salmonella* may be effective against *Salmonella* infections.

DESCRIPTORS: Animal models; Effector cells; Enzyme-linked immunosorbent assay; Feces; Flagellin; Genetic engineering; Immunoglobulin A; Infection; Infectious diseases; Lymphoid tissue; Mucosal immunity; Typhoid fever; Vaccination; Vaccines; *Bifidobacterium animalis*; *Salmonella typhimurium*

30/3, K/18 (Item 1 from file: 34)  
DIALOG(R) File 34: SciSearch(R) Cited Ref Sci  
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13296411 Genuine Article#: 864V6 No. References: 29  
Title: Mucosal administration of flagellin induces innate immunity in the mouse lung  
Author(s): Honko AN; Mzel SB (REPRINT)  
Corporate Source: Wake Forest Univ, Sch Med, Dept Microbiol & Immunol, Med Ctr Blvd/Winston Salem/NC/27157 (REPRINT); Wake Forest Univ, Sch Med, Dept Microbiol & Immunol, Winston Salem/NC/27157 (smzel@wubmc.edu)  
Journal: INFECTION AND IMMUNITY, 2004, V72, N11 (NOV), P6676-6679  
ISSN: 0019-9567 Publication date: 20041100  
Publisher: AMER SOC MICROBIOLOGY, 1752 N ST NW WASHINGTON, DC 20036-2904 USA  
Language: English Document Type: ARTICLES (ABSTRACT AVAILABLE)

Title: Mucosal administration of flagellin induces innate immunity in the mouse lung  
Abstract: Nonsurgical intratracheal instillation of 1 mug of purified, recombinant flagellin in several strains of mice stimulated a transient innate immune response in the lung characterized by the infiltration of neutrophils and the rapid production of tumor necrosis factor alpha, interleukin 6, granulocyte colony-stimulating factor, and the chemokines keratinocyte-derived chemokine, MIP1alpha, and MIP-2.  
... Identifiers--GRAM NEGATIVE FLAGELLIN; INDUCED PULMONARY INFLAMMATION; SYNTHETIC RECOMBINANT VACCINE; PROMONOCYTIC CELL-LINE; NECROSIS-FACTOR-ALPHA; BACTERIAL FLAGELLIN; SALMONELLA-TYPHIMURIUM; MICE; INDUCTION; EXPRESSION

30/3, K/19 (Item 2 from file: 34)  
DIALOG(R) File 34: SciSearch(R) Cited Ref Sci  
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05533938 Genuine Article#: WE900 No. References: 21  
Title: Safety of live oral *Salmonella typhi* vaccine strains with  
Page 51

FLAGELLIN10585880.txt

deletions in htrA and aroC aroD and immune response in humans

Author(s): Tacket CO (REPRINT); Sztajn MB; Losonsky GA; Wasserman SS; Nataro JP; Edelman R; Pickard D; Dougan G; Chatfield SN; Levine MM  
Corporate Source: UNI V MARYLAND, SCH MED, CTR VACCINE DEV, DEPT MED, 685 W BALTIMORE ST/ BALTIMORE/ MD 21201 (REPRINT); UNI V MARYLAND, SCH MED, CTR VACCINE DEV, DEPT PEDIAT/ BALTIMORE/ MD 21201; UNI V LONDON IMPERIAL COLL SCI TECHNOL & MED, DEPT BIOCHEM/ MEDICA GRP RES, VACCINE RES UNIT/ LONDON SW1 2AZ/ ENGLAND/

Journal: INFECTION AND IMMUNITY, 1997, V65, N2 (FEB), P452-456

ISSN: 0019-9567 Publication date: 19970200

Publisher: AMER SOC MICROBIOLOGY, 1325 MASSACHUSETTS AVENUE, NW WASHINGTON, DC 20005-4171

Language: English Document Type: ARTICLES (ABSTRACT AVAILABLE)

Title: Safety of live oral *Salmonella typhi* vaccine strains with deletions in htrA and aroC aroD and immune response in humans

Abstract: A single-dose, oral *Salmonella typhi* vaccine strain has been sought as a carrier or vector of cloned genes encoding protective antigens of other pathogens. Such a hybrid vaccine, administered orally, would stimulate immune responses both at the mucosal surface and in the systemic compartment and would potentially provide protection against multiple pathogens. S...

...5 x 10(7) to 5 x 10(9) CFU with buffer, and safety and immune responses were assessed. CVD 908-htrA and CVD 906-htrA were well tolerated in volunteers; mild...

...36 volunteers and mild fever in 1 volunteer were the only notable adverse responses. The vaccine strains were not detected in blood cultures and only transiently detected in stool. Serum immune responses to *S. typhi* lipopolysaccharide and H antigens were observed in 75 to 100% of volunteers...

...either strain, Sixty three percent to 83% of volunteers developed lymphoproliferative responses to *S. typhi* flagellar and particulate antigens after the higher doses. These studies demonstrate the potential of CVD 908-htrA...

...Identifiers--ESCHERICHIA-COLI; DELTA-AROC; TYPHI MURIMUMMUNOGENICITY; CONSTRUCTION; VOLUNTEERS; MICE; CVD-908; PROTEIN; MUTANT

30/3, K/20 (Item 3 from file: 34)  
DIALOG(R) File 34: SciSearch(R) Cited Ref Sci  
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04506807 Genuine Article#: TH744 No. References: 48  
Title: SYNTHETIC RECOMBINANT VACCINES AGAINST VIRAL AGENTS

Author(s): ARNON R; LEVI R

Corporate Source: WEIZMANN INST SCI, DEPT CHEM IMMUNOL/ IL-76100 REHOVOT/ ISRAEL/

Journal: INTERNATIONAL ARCHIVES OF ALLERGY AND IMMUNOLOGY, 1995, V108, N4 (DEC), P321-326

ISSN: 1018-2438

Language: ENGLISH Document Type: ARTICLES (Abstract Available)

...Abstract: the genome of a desired vector, using recombinant DNA technology. The results discussed indicate that immunization with such vaccines carrying viral epitopes may lead to protective immunity against viral agents. Oligonucleotides coding for three influenza epitopes stimulating B cells, T helper cells and

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cytotoxic lymphocytes were individually inserted into the flagellin gene of a *Salmonella* vaccine strain. Immunization of mice with the resultant recombinant bacteria or their isolated flagella induced a specific mucosal anti-influenza protective response. The most efficient vaccine consisted of all three recombinant flagella, administered intranasally. The protection elicited was cross-strain specific, long-lasting and efficient against a...  
...Identifiers--INFLUENZA-A VIRUS; TOXIC LYMPHOCYTES-T; SALMONELLA-TYPHIMURIUM; ESCHERICHIA-COLI; IMMUNE-RESPONSE; CHOLERA-TOXIN; CELL EPI TOPE; PROTECTION; INFECTION; PROTEIN  
...Research Fronts: INDUCTION OF CD8+ CYTOTOXIC T-LYMPHOCYTES; HEPATITIS-B VIRUS NUCLEOCAPSID PROTEIN; HIV-1 DERIVED PEPTIDE VACCINE; CLASS-I MHC-RESTRICTED CTL EPI TOPES)

30/3, K/21 (Item 1 from file: 72)  
DI ALCO (R) File 72: EMBASE  
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0080790762 EMBASE No: 2005435380

Cellular mechanisms of the adjuvant activity of the flagellin component FljB of *Salmonella enterica* serovar typhimurium to potentiate mucosal and systemic responses  
Pino O.; Martin M.; Mchalek S.M.  
Department of Pediatric Dentistry, University of Alabama at Birmingham  
Birmingham AL 35294, United States  
AUTHOR EMAIL: suemch@ab.edu  
CORRESP. AUTHOR AFFIL: Mchalek S.M.: Department of Microbiology,  
University of Alabama at Birmingham, BBRB 258/5, 845 19th Street South,  
Birmingham AL 35294-2170, United States  
CORRESP. AUTHOR EMAIL: suemch@ab.edu

Infection and Immunity (Infect. Immun.) (United States) October 1, 2005, 73/10 (6763-6770)

CODEN: INFI B ISSN: 0019-9567

DOI: 10.1128/IAI.73.10.6763-6770.2005

DOCUMENT TYPE: Journal; Article RECORD TYPE: Abstract

LANGUAGE: English SUMMARY LANGUAGE: English

NUMBER OF REFERENCES: 42

Cellular mechanisms of the adjuvant activity of the flagellin component FljB of *Salmonella enterica* serovar typhimurium to potentiate mucosal and systemic responses

An expanding area of interest is the utilization of microbe-based components to augment mucosal and systemic immune responses to target antigens. Thus, the aim of the present study was to assess if the flagellin component FljB from *Salmonella enterica* serovar Typhimurium could act as a mucosal adjuvant and then to determine the cellular mechanism(s) by which FljB mediates its adjuvant properties. To determine if FljB could act as a mucosal adjuvant, mice were immunized by the intranasal (i.n.) route with antigen alone or in conjunction with FljB. Additionally ...

...cells by flow cytometry and determined the functional role these costimulatory molecules played in the adjuvant properties of FljB in vivo. Mice immunized by the i.n. route with antigen and FljB exhibited significantly elevated levels of mucosal and systemic antibody and CD4<sup>+</sup> T-cell responses compared to mice given antigen only. Stimulation of dendritic cells in vitro with FljB resulted in a pronounced increase in the surface...

...The percentage of dendritic cells expressing B7-2 but not B7-1 increased

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significantly when stimulated with FljB over a concentration range of 10 to 10,000 ng/ml. Immunization of wild-type and B7-1, B7-2, and B7-1/2 knockout mice by...

...that the ability of FljB to increase B7-2 expression is largely responsible for its adjuvant effect in vivo. These findings demonstrate that FljB can act as an effective mucosal adjuvant and that its ability to enhance the level of B7-2 expression is predominantly responsible for its adjuvant properties. Copyright (c) 2005, American Society for Microbiology. All Rights Reserved.

#### DRUG DESCRIPTIONS:

...protein--drug development--dv; \*bacterial protein--drug dose--do; \*bacterial protein--intranasal drug administration--na; \*flagellin; \*immunological adjuvant--drug development--dv; \*immunological adjuvant--drug dose--do; \*immunological adjuvant--intranasal drug administration--na; \*salmonellosis vaccine--drug development--dv; \*salmonellosis vaccine--drug dose--do; \*salmonellosis vaccine--intranasal drug administration--na

#### MEDICAL DESCRIPTIONS:

animal cell; animal experiment; antibody response; article; controlled study; dendritic cell; drug efficacy; drug purification; drug response; flow cytometry; immunization; knockout mouse; mouse; mucosal immunity; nonhuman; priority journal; protein expression; protein function; T lymphocyte

CAS REGISTRY NO.: 12777-81-0 (flagellin)

#### SECTION HEADINGS:

Immunology, Serology and Transplantation

Drug Literature Index

Microbiology: Bacteriology, Mycology, Parasitology and Virology

30/3, K/22 (Item 2 from file: 72)

DIALOG(R) File 72: EMBASE

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0077253128 EMBASE No: 1998163286

Immunization against the colonization factor antigen I of enterotoxigenic *Escherichia coli* by administration of a bivalent *Salmonella typhimurium* aroA strain

Gillobel H.C.R.; Luna M.G.; Camacho E.F.; Almeida D.F.; Ferreira L.C.S. Lab. de Fisiologia Celular, Inst. de Biofis. Carlos Chagas Filho, Univ. Federal do Rio de Janeiro, Rio de Janeiro, RJ, Brazil; Depto. de Biofis. e Biometria, Instituto de Biologia, Univ. do Estado do Rio de Janeiro, Rio de Janeiro, RJ, Brazil; Departamento de Genética, Instituto de Biologia, Univ. Federal do Rio de Janeiro, Rio de Janeiro, RJ, Brazil

AUTHOR EMAIL: lcsf@bccf.biof.ufrj.br

CORRESP. AUTHOR/AFFILI: Ferreira L.C.S.: Laboratório de Fisiologia Celular, Instituto de Biofísica Carlos Chagas Filho, OCS, UFRJ, 21941-590 Rio de Janeiro, RJ, Brazil

Brazilian Journal of Medical and Biological Research (Braz. J. Med.

Biol. Res.) (Brazil) April 1, 1998, 31/4 (545-554)

CODEN: BBJPMB ISSN: 0100-879X

DOCUMENT TYPE: Journal; Article RECORD TYPE: Abstract

LANGUAGE: English SUMMARY LANGUAGE: English

NUMBER OF REFERENCES: 32

Immunization against the colonization factor antigen I of enterotoxigenic *Escherichia coli* by administration of a bivalent *Salmonella typhimurium* aroA strain

...CFA/II subunit was constructed and used to transform a derivative of the attenuated *Salmonella typhimurium* aroA vaccine strain

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SL3261 carrying an F1acI(q). Treatment of the transformed strain with isopropyl-beta-D-thiogalactopyranoside (IPTG) resulted in elevated in vitro expression of the CFA/I subunit. Although flagellar function and lipopolysaccharide (LPS) synthesis were similar in both the parental and the recombinant strains...

...the same mice developed anti-LPS IgA ( $P < 0.05$ ). The results indicate that the vaccine strain elicited an antibody response against the bacterial host both after oral and intravenous immunization while the response against the CFA/I antigen was significant only after inoculation by the intravenous route.

DRUG DESCRIPTIONS:

\*adhesin--endogenous compound--ec; \*escherichia coli enterotoxin; \*typhoid vaccine--drug development--dv; \*typhoid vaccine--pharmaceuticals  
--pr  
escherichia coli lipopolysaccharide; glucopyranoside; immunoglobulin  
a--endogenous compound--ec

MEDICAL DESCRIPTIONS:

\*bacterial colonization; \*immunization; \*salmonella typhimurium  
; \*vaccine production  
animal experiment; animal tissue; antibody response; antigen  
expression; article; controlled study; fimbria; flagellum genetic  
engineering; inoculation; intravenous drug administration; male; mouse;  
mucosal immunity; nonhuman; oral drug administration

SECTION HEADINGS:

Immunology, Serology and Transplantation

Drug Literature Index

Pharmacy

Microbiology: Bacteriology, Mycology, Parasitology and Virology

30/3, K/23 (Item 1 from file: 144)

DIALOG(R) File 144: Pascal

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18101092 PASCAL No.: 07-0178829

Flagellin-induced tolerance of the Toll-like receptor 5 signaling pathway in polarized intestinal epithelial cells

JUN SUN; FEGAN Pamela E; DESAI Anjali S; MADARA James L; HOBERT Michael E  
Department of Pathology, The University of Chicago, Chicago, Illinois,  
United States

Journal: American journal of physiology. Gastrointestinal and liver  
physiology, 2007, 55 (3) G767-G778

Language: English

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Flagellin-induced tolerance of the Toll-like receptor 5 signaling pathway in polarized intestinal epithelial cells

-Salmonella typhimurium is a gram-negative enteric pathogen that invades the mucosal epithelium and is associated with diarrheal illness in humans. Flagellin from S. typhimurium and other gram-negative bacteria has been shown to be the predominant proinflammatory mediator through...

...basolateral Toll-like receptor 5 (TLR5). Recent evidence has shown that prior exposure can render immune cells tolerant to subsequent challenges by TLR ligands. Accordingly, we examined whether prior exposure to purified flagellin would render human intestinal epithelial cells insensitive to future contact. We found that flagellin-induced tolerance is common to polarized epithelial cells and prevents further activation of proinflammatory signaling cascades by

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both purified flagellin and Salmonella bacteria but does not affect TNF- $\alpha$  stimulation of the same pathways. Flagellin tolerance is a rapid process that does not require protein synthesis, and that occurs within 1 to 2 h of flagellin exposure. Prolonged flagellin exposure blocks activation of the NF- $\kappa$ B, MAPK, and phosphoinositol 3-kinase signaling pathways and...

... the basolateral TLR5 without affecting the polarity or total expression of TLR5. After removal of flagellin, cells require more than 24 h to fully recover their ability to mount a normal proinflammatory response. We have found that activation of phosphoinositol 3-kinase and Akt by flagellin has a small dampening effect in the early stages of flagellin signaling but is not responsible for tolerance. Our study indicates that inhibition of TLR5-associated IL-1 receptor-associated kinase-4 activity occurs during the development of flagellin tolerance and is likely to be the cause of tolerance.

30/3, K/24 (Item 1 from file: 156)  
DI ALCO (R) File 156: ToxFile  
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1023710 NLM Doc No: CRI SP/2003/ AI 056172-010001 Sec. Source ID:  
CRI SP/2003/ AI 056172-010001

T Cell Response to Listeria Monocytogenes Infection  
LEFFRANCO S LJJR  
llefranc@and.uchc.edu, UNIV OF CONNECTICUT HEALTH CTR, 263 FARMINGTON  
AVENUE, FARMINGTON, CT 06030

Source: Crisp Data Base National Institutes of Health  
City or State: CONNECTICUT Zip Code: 06030  
Pub. Year: 2003

Sponsoring Agency: U.S. DEPT. OF HEALTH AND HUMAN SERVICES; PUBLIC HEALTH  
SERVICE; NATIONAL INSTITUTES OF HEALTH; NATIONAL INSTITUTE OF ALLERGY AND  
INFECTIOUS DISEASES

Award Type: Grant  
Document type: Research  
Languages: ENGLISH  
Record type: Completed

#### T Cell Response to Listeria Monocytogenes Infection

The factors essential to induction of a protective immune response to bacterial infections are incompletely understood. In the case of Listeria monocytogenes (LM) infection, T cells are required to effect sterilizing immunity. However, vaccination with heat killed LM (HKL) results in poor protective immunity but the basis for this finding is unknown. Using live and HK LM inoculation we have begun to dissect the requirements for the initiation of the T cell immune response. Preliminary results indicate that HKL immunization induces rapid, but essentially abortive, T cell activation. From this and other data, we hypothesize...

... quality of the initial T cell-antigen-presenting cell (APC) interaction is impaired in HKL immunization. Therefore, this system can be used to dissect the early steps leading to a productive immune response and subsequent protective immunity. The overall goal of this proposal is to understand the requirements for initiation of a productive T cell response and to utilize costimulator agonism and bacterial adjuvants to promote vaccination. The aims of the...

... versus live LM vaccination. Aim 2. To determine the requirements CD4 T cell help and TLR signaling for optimal T cell responses to LM infection. Aim 3. To determine the ability...

Identifiers: laboratory mouse; genetically modified animal; Salmonella



FLAGELLIN10585880.txt

typhimurium; Listeria infection; biological signal transduction;  
dendritic cell; T lymphocyte; helper T lymphocyte; cell cell interaction;  
antigen presenting cell; leukocyte activation /transformation; active  
immunization; enzyme linked immunosorbent assay;  
immunofluorescence technique; bacterial antigen; immunomodulator %  
% macroorganism immunology; attenuated macroorganism virulence;  
flagellin; confocal scanning microscopy; gene targeting;  
mucosal immunity; bioterrorism /chemical warfare; toll like  
receptor

30/3, K/25 (Item 2 from file: 156)  
Dialog File 156: ToxFile  
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1023709 NLM Doc No: CRI SP/2003/ AI 056172-01 Sec. Source ID:  
CRI SP/2003/ AI 056172-01  
Modulation of Biodefense Responses to Bacterial Pathogen  
LEFRANCOIS LJ  
LLEFRANCOIS@URON.UCHC.EDU, UNIV OF CONNECTICUT HEALTH CTR, 263 FARMINGTON  
AVENUE, FARMINGTON, CT 06030  
Source: Crisp Data Base National Institutes of Health  
City or State: CONNECTICUT Zip Code: 06030  
Pub. Year: 2003  
Sponsoring Agency: U.S. DEPT. OF HEALTH AND HUMAN SERVICES; PUBLIC HEALTH  
SERVICE; NATIONAL INSTITUTES OF HEALTH; NATIONAL INSTITUTE OF ALLERGY AND  
INFECTIOUS DISEASES  
Award Type: Grant  
Document type: Research  
Languages: ENGLISH  
Record type: Completed

... project application "Modulation of biodefense responses to bacterial  
pathogens" is proposed from the Division of Immunology, U.  
Connecticut Health Center. This program is composed of three projects and  
three cores focused on the immune response to bacteria and  
their products, all of which are included as category B entities on...

... Program list. The program theme is to define the parameters for  
initiation of anti-microbial immune responses and also examines  
bacterial products in promoting immunity, or in the case of  
enterotoxins, pathology, in mucosal tissues. The central hypothesis  
is that early events in T cell-antigen presenting cell (APC) interactions  
determine whether or not long-term immunity is induced in  
response to vaccination, or whether damage is initiated in  
response to a bacterial toxin. Each project focuses on a unique  
aspect of the theme to advance our understanding of the immune  
response to bacterial antigens. Project 1 (Lefrancois) proposes to  
investigate the T cell response to live or heat killed Listeria  
monocytogenes. T cell-APC interactions will be examined as will the  
role of T cell help and Toll-like receptors in optimizing the  
response. Experiments testing augmentation of the response by  
bacterial products or costimulatory agonists will be performed in  
collaboration with the other two projects. Project 2 (McSorley) is focused  
on the CD4 T cell response to Salmonella typhimurium  
flagellin and will test whether flagellin can activate APC in  
vivo and thus be an effective adjuvant or vaccine. Project 3  
(Vella) aims to define how staphylococcal enterotoxin B (SEB) influences  
APC function via T cell interactions and will develop a model of lung  
mucosa injury to SEB insult. Components of all three projects are  
aimed at examining T cell-APC interactions following infection or toxin  
challenge and the innate immune response is also a common  
topic. These studies provide a natural bridge towards the goal of

augmentation of protective immunity. The projects utilize in vivo models and in-depth cellular immunological techniques and are supported by 3 cores: administrative, flow cytometry and fluorescence microscopy/immunohistochemistry. The projects and cores synergistically interact and mutually reinforce one another to achieve the goal...

... the program Coupled with strong institutional support, it is anticipated that significant new insights in immune response regulation to pathogens and their byproducts will be obtained.  
Identifiers: T lymphocyte; cell cell interaction; antigen presenting cell; active immunization; bacterial antigen; immunomodulator; microorganism immunology; attenuated microorganism virulence; bioterrorism/chemical warfare

30/3, K/26 (Item 1 from file: 370)  
DI ALCO (R) File 370: Science  
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00509951 (USE 9 FOR FULLTEXT)  
Helicobacter pylori Virulence and Genetic Geography  
Covacci, Antonello; Telford, John L.; Del Giudice, Giuseppe; Parsonnet, Julie; Rappuoli, Rino<ORF RID="C1">  
IRIS, Chiron SpA, Via Fiorentina 1, 53100 Siena, Italy. Department of Medicine/Infectious Diseases Hpt T152, Stanford University, CA 94305, USA

Science Vol. 284 5418 pp. 1328  
Publication Date: 5-21-1999 (990521) Publication Year: 1999  
Document Type: Journal ISSN: 0036-8075  
Language: English  
Section Heading: REVIEWS  
Word Count: 4111

(THIS IS THE FULLTEXT)

...Text: minimal set of metabolic genes (B2). The mechanisms for environmental adaptation such as the stringent response and the two-component regulatory systems are absent or rare, respectively (B3). For example, Pseudomonas...Hp: duodenal ulcer, gastric ulcers, adenocarcinoma of the distal stomach (antrum and fundus), and gastric mucosa-associated lymphoid tissue (MALT) lymphoma. Taken together, each year, at least 7 million cases of...

...and survival in the human stomach. Most notable among these factors are the urease and flagella. Urease metabolizes urea to carbon dioxide and ammonia to buffer the gastric acid. Flagella allow the bacterium to swim across the viscous gastric mucus and reach the more neutral pH below the mucus. Knockout mutants of the urease or flagellar genes are defective in colonization in a gnotobiotic piglet model of infection (B16 the fucosylated Lewis x and Lewis y blood group antigens expressed on the gastric mucosa. This antigenic mimicry may result in immune tolerance against antigens of the pathogen or in induction of autoantibodies that recognize gastric epithelial...

...activate neutrophils and may be involved in the recruitment of these cells to the gastric mucosa and hence may contribute to the inflammatory response (B20)...Both systems evolved possibly by gene duplication from transmembrane structures with extracellular, tubular protrusions (the flagellum and the conjugative pilus, respectively) and mediate communication processes between cells by delivering macromolecular messengers. The challenge to develop a vaccine has been particularly successful in mouse models with either the Hp-related

species-*Helicobacter felis* (B36) - or the mouse-adapted Hp that mimics human infection (B32) (B37) . Vaccine-induced protection from infectious challenge and eradication of established infection have been proved with many...

...lysates, and several purified antigens (B36) (B38) (Table 2). The most successful approach has been mucosal immunization with adjuvants such as cholera or *E. coli* enterotoxins or the genetically detoxified derivative, LTK6...

...a role for CD8.sup(+) cells has also been evoked (B44) . Whereas CD4.sup(+)-mediated immunity is a common mechanism of protection against intracellular parasites, it is an unusual mechanism to induce immunity against a bacterium that remains in the extracellular environment...

...A major question is why immunization would be successful if the natural immune response does not clear the infection. There is evidence showing that the majority of CD4.sup...

...specific for CagA. This suggests that Hp infection induces an interferon- (gamma) (Th1)-mediated proinflammatory response that is not able to eliminate the bacteria. It is possible that vaccination triggers a Th2 immune response capable of mediating protection (B45)... Reported virulence factors.

Factor	Function	Distribution	Reference
Urease	Buffers stomach acid	All strains	Reference B51
Flagella	Motility	All strains	Reference
B52			
NAP	Neutrophil activation	All strains	Reference B20
BabA	Adhesion for...		
...PAI	31 genes coding for type IV secretion system	Type I strains	Reference B26
CagA	Immunodominant antigen (part	Type I strains	Reference
B33	of cag PAI)		
PilB	Equivalent to CagE	Type...	
... Figure	Removed		

Begin Table : Columns 1 - 5 of 5

Caption:

*Helicobacter pylori* antigens, vaccine formulations, and routes of administration proven efficacious in animal models of infection. Hp antigens that...

...felis, because of the conservation of these proteins. Most of these antigens have been given mucosally, more often orally, in association with mucosal adjuvants such as CT and LT or the genetically inactivated LT mutant LTK63 Reference B37 Reference B39 . More recently, other mucosal routes have been tested Reference B56 . Finally, the parenteral route of immunization has been shown to represent a potentially feasible approach Reference B40 .

Animal model	<i>H. pylori</i> antigen(s)	Adjuvant or vector	Route	Infection with
Prophylactic vaccination				
Mouse	Whole-cell	CT, LT, LTK63...		

...in	Hf, Hp	Saponin derivative	sc	Hp
	UreB subunit	CT, LT	os	Hf, Hp
	HspA	S. typhimurium	in	Hp
	HspB	CT, LT	os	Hf
	UreB...	CT, LT, LTK63	os	Hf, Hp

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01952748 ORDER NO: AADAA-13090964  
 Host responses to Salmonella typhimurium infection in vitro and in vivo

Author: Bergman, Molly Ann  
 Degree: Ph. D.  
 Year: 2003  
 Corporate Source/Institution: University of Washington (0250)  
 Source: VOLUME 64/05-B OF DISSERTATION ABSTRACTS INTERNATIONAL.  
 PAGE 2018. 125 PAGES

Host responses to Salmonella typhimurium infection in vitro and in vivo

...localized and systemic disease of significant morbidity and mortality; disease can be prevented by oral immunization with viable attenuated bacteria. During the *Salmonella*-host interaction, multiple processes occur that...

...bacterial induction of programmed host cell death, innate recognition of bacterial motifs, and adaptive immune responses to microbial antigens.

Prior studies observed *Salmonella* invasion of macrophages induced apoptosis...

...*Salmonella* infection, CD4+ T cells respond to FlhC, the major subunit protein of the flagellar apparatus. Described here is further examination of the CD4+ T cell response to FlhC and identification of four discrete FlhC epitopes with varying immunodominance *in vitro* and *in vivo*. Analysis of CD4+ T cell responses...

...unique surface organelles as a rich source of natural antigens. *Salmonella* antigens directly stimulated Toll-like receptors (TLRs) or were intimately associated with TLR ligands, suggesting that TLR recognition biases T cell responses to specific antigens. *Salmonella* evaded innate and adaptive immune recognition by modifying or repressing expression of natural antigens during growth *in vivo*...

...Experimental dysregulation of FlhC expression during *in vivo* infection profoundly influenced the ensuing mucosal CD4+ T cell response to FlhC, indicating that *Salmonella* preferentially expresses FlhC during colonization of the mucosa. These results demonstrate that regulated antigen expression can influence antigen-specific immune responses, and may enable *Salmonella* to evade immune recognition and continue replication in host tissue.

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0000950121 (USE FORMAT 7 OR 9 FOR FULLTEXT)  
Researchers at University Federal of Sao Paulo target malaria vaccines  
Biotech Business Week, December 29, 2008, p.1536

DOCUMENT TYPE: Expanded Reporting LANGUAGE: English  
RECORD TYPE: FULLTEXT  
WORD COUNT: 445

...TEXT: malaria are presented in the report 'New malaria vaccine candidates based on the Plasmodium vivax Merozoite Surface Protein-1 and the TLR-5 agonist Salmonella Typhimurium FlhC flagellin.' "The present study evaluated the immunogenicity of new malaria vaccine formulations based on the 19kDa C-terminal fragment of Plasmodium vivax Merozoite Surface Protein-1 (MSP1(19)) and the Salmonella enterica serovar Typhimurium flagellin (FlhC), a Toll-like receptor 5 (TLR5) agonist (see also Malaria Vaccines). FlhC was used as an adjuvant either admixed or genetically linked to the P. vivax MSP1(19) and administered to C57BL/6 mice via parenteral (s.c.) or mucosal (i.n.) routes," scientists in Sao Paulo, Brazil report. "The recombinant fusion protein preserved MSP1(19) epitopes recognized by sera collected from P. vivax infected humans and... activity. Mice parenterally immunized with recombinant P. vivax MSP1(19) in the presence of FlhC, either admixed or genetically linked,

elicited strong and long-lasting MSP1(19)-specific systemic antibody responses...

...prevailing IgG1 subclass response. Incorporation of another TLR agonist, CpG CDN 1826, resulted in a more balanced response, as evaluated by the IgG1/IgG2c ratio, and higher cell-mediated immune response measured by interferon-gamma secretion. Finally, we show that MSP1(19)-specific antibodies recognized the native protein expressed on the surface of *P. vivax* parasites harvested from...

...class of malaria vaccine formulation based on the use of malarial antigens and the innate immunity agonist FliC," wrote D.Y. Bargieri and colleagues, University Federal of Sao Paulo. The researchers concluded: "It contains intrinsic adjuvant properties and enhanced ability to induce specific humoral and cellular immune responses when administered alone or in combination with other adjuvants." Bargieri and colleagues published their study in *Vaccine* (New malaria vaccine candidates based on the *Plasmodium vivax* Merozoite Surface Protein-1 and the TLR-5 agonist *Salmonella* Typhimurium FliC flagellin. *Vaccine* 2008;26(48):6132-42). For additional information, contact D. Y. Bargieri, Universidade Federal de Sao Paulo, Centro Interdisciplinar de Terapia Genica (CINTERGEN), Escola Paulista de Medicina ...

...for the journal *Vaccine* is: Elsevier Science Ltd., the Boulevard, Langford Lane, Kidlington, Oxford OX5 1GB, Oxon, England. Keywords: Brazil, Sao Paulo, Biotechnology, Drug Development, Immunization, Malaria Vaccines, *Plasmodium vivax*, *Salmonella*, Therapy, Treatment, Tropical Disease, Vaccination. This article was prepared by Biotech Business Week editors from staff and other reports. Copyright 2008, Biotech...

DESCRIPTORS: Brazil; Sao Paulo; Biotechnology; Drug Development; Immunization; Malaria Vaccines; *Plasmodium vivax*; *Salmonella*; Therapy; Treatment; Tropical Disease; VaccinationAll News; Professional News

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0000313398 (USE FORMAT 7 OR 9 FOR FULLTEXT)  
Researchers' data from Cuba, the South Korea and the United States advance vaccines research  
*Cancer Vaccine Week*, June 26, 2006, p. 85

DOCUMENT TYPE: Expanded Reporting LANGUAGE: English  
RECORD TYPE: FULLTEXT  
WORD COUNT: 946

...TEXT: United States.

Study 1: Very small size proteoliposomes derived from *Neisseria meningitidis* are an effective adjuvant for generation of CTL responses to peptide and protein antigens.

"The development of potent adjuvants, conditioning innate and adaptive immunity, particularly CTL responses, has become currently a hot point in the rational design of vaccines for cancer immunotherapy. We have described a new approach, in which gangliosides are incorporated into vesicles from *Neisseria*...

...and F3II tumor models respectively," said Circe Mesa and colleagues at the Center of Molecular Immunology in Havana. "Also VSSP induces activation of CTL responses to co-injected trimmed peptides and...

...T cells for primary CD8 T cells expansion."

Mesa and associates published their study in Vaccine (Very small size proteoliposomes derived from *Neisseria meningitidis*: An effective adjuvant for generation of CTL responses to peptide and protein antigens. Vaccine, 2006;24(14):2692-2699).

For additional information, contact Circe Mesa, Vaccine Department, Center for Molecular Immunology, 216 Esq 15, Atabey, Playa, C Habana 16040, Cuba. circe@ct.cim.sld.cu.

Study 2: A bacterial flagellin, *Vibrio vulnificus* FlaB, has a strong mucosal adjuvant activity to induce protective immunity.

"Flagellin, the structural component of flagellar filament in various locomotive bacteria, is the ligand for Toll-like receptor 5 (TLR5) of host cells. TLR stimulation by various pathogen-associated molecular patterns leads to activation of innate and subsequent adaptive immune responses. Therefore, TLR ligands are considered attractive adjuvant candidates in vaccine development. In this study, we show the highly potent mucosal adjuvant activity of a *Vibrio vulnificus* major flagellin (FlaB)," investigators in South Korea report.

"Using an intranasal immunization mouse model, we observed that co-administration of the flagellin with tetanus toxoid (TT) induced significantly enhanced TT-specific immunoglobulin A (IgA) responses in both mucosal and systemic compartments and IgG responses in the systemic compartment," said Shee Eun Lee at Chonnam National University and collaborators in South Korea. "The mice immunized with TT plus FlaB were completely protected from systemic challenge with a 200x minimum lethal..."

...number of TLR5-expressing cells in cervical lymph nodes."

They concluded, "These results indicate that flagellin would serve as an efficacious mucosal adjuvant inducing protective immune responses through TLR5 activation."

Lee and associates published their study in Infection and Immunity (A bacterial flagellin, *Vibrio vulnificus* FlaB, has a strong mucosal adjuvant activity to induce protective immunity. Infect Immun, 2006;74(1):694-702).

For additional information, contact Joon Haeng Rhee, National Research Laboratory...

...Dong-Ku, Gwangju 501-746, South Korea. jhrhee@chonnam.chonnam.ac.kr.

Study 3: Active immunization with a detoxified endotoxin vaccine protects against lethal polymicrobial sepsis.

Researchers in the United States report, "An experimental vaccine for sepsis, composed of detoxified *Escherichia coli* J5 lipopolysaccharide (LPS) complexed with the outer membrane..."

...core glycolipid antibody and has been tested in pilot studies in human volunteers."

"Mice were immunized with the LPS-J5/OMP vaccine with or without synthetic oligodeoxynucleotides (ODNs) containing unmethylated CpG motifs as a vaccine adjuvant (CpG ODN). The efficacy of the vaccine-induced antibody response was tested in a cecal ligation and puncture model," said Steven M Opal at Brown University and collaborators.

"Immunization resulted in a >20-fold increase in anti-core glycolipid antibody levels, which were further..."

...ODN, compared with the levels in mice in the control group," the researchers reported. "The vaccine provided a survival advantage after a cecal ligation and puncture was performed ( $p < 0.01$ ) and significantly decreased the levels of bacteria in organs."

FLAGELLI N10585880.txt

Immunoglobulin G (IgG) anti-core glycolipid antibodies were decreased in mice to a significantly greater extent than were levels of total circulating IgG or IgG to the OMP part of the vaccine complex, suggesting specific epitope binding and clearance."

They concluded, "These results indicate that the detoxified LPS-J5/OMP vaccine induces high levels of antibody against the core glycolipid of LPS and functions in vivo..."

...sepsis."

Opal and his coauthors published their study in the Journal of Infectious Diseases (Active immunization with a detoxified endotoxin vaccine protects against lethal polymicrobial sepsis: its use with CpG adjuvant and potential mechanisms. J Infect Dis, 2005; 192(12):2074-2080).

For additional information, contact...

...Opal@rown.edu.

Keywords: Providence, Rhode Island, United States, Septicemia Vaccine, Sepsis, Septic Shock, Vaccine Development, Vaccine Efficacy, Vaccine Adjuvant, Immunology, Immunotherapy, Neisseria Meningitidis, Oligonucleotides, Proteomics.

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DESCR PTORS: Cancer Vaccine; Immunology; Immunotherapy; Neisseria Meningitidis; Oligonucleotides; On; Proteomics; Providence; Rhode Island; Sepsis; Septic Shock; Septicemia Vaccine; United States; Vaccine Adjuvant; Vaccine Development; Vaccine Efficacy; Vaccines; All News

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0000311462 (USE FORMAT 7 OR 9 FOR FULLTEXT)  
New research from Cuba, the South Korea and the United States in the area of vaccines detailed  
Cancer Vaccine Week, June 19, 2006, p.44

DOCUMENT TYPE: Expanded Reporting LANGUAGE: English  
RECORD TYPE: FULLTEXT  
WORD COUNT: 945

...TEXT: vaccines data.

Study 1: Very small size proteoliposomes derived from Neisseria meningitidis are an effective adjuvant for generation of CTL responses to peptide and protein antigens.

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...T cells for primary CD8 T cells expansion."  
Mesa and associates published their study in Vaccine (Very small



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DESCRIPTORS: Cancer Vaccine; Immunology; Immunotherapy; Neisseria Meningitidis; Oligonucleotides; On; Proteomics; Providence; Rhode Island; Sepsis; Septic Shock; Septicemia Vaccine; United States; Vaccine Adjuvant; Vaccine Development; Vaccine Efficacy; Vaccines; All News; All News

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0000209888 (USE FORMAT 7 OR 9 FOR FULLTEXT)  
Findings in salmonella vaccines provide new insights  
Immunotherapy Weekly, April 27, 2005, p.242

DOCUMENT TYPE: Expanded Reporting LANGUAGE: English  
RECORD TYPE: FULLTEXT  
WORD COUNT: 1217

...TEXT: on salmonella vaccines.

Study 1: The absence of the substance P receptor resulted in enhanced immunoglobulin A response and protection against Salmonella enterica.

... of the neurokinin-1 receptor-deficient (NK1R -/-) mouse permitted inquiry into the regulation of secretory immunoglobulin A (S-IgA) responses by substance P (SP) after oral immunization with a Salmonella enterica serovar Typhimurium vector expressing colonization factor antigen I (CFA/I) from enterotoxigenic Escherichia coli. In NK1R -/- mice, mucosal and serum IgA anti-CFA/I fibrial responses were augmented, while secreted IgG anti-CFA...

...the augmented S-IgA responses occurred, minimally, the responses were not attributed to differences in vaccine colonization of Peyer's patch (PP) and spleen or in their respective tissue weights," said...

...proinflammatory responses to Salmonella infections."

Walters and her coauthors published their study in Infection and Immunity (Enhanced immunoglobulin A response and protection against Salmonella enterica serovar Typhimurium in the

absence of the substance P receptor. Infect Immun, 2005; 73(1):317-324).

For more information, contact David W Pascual, Veterinary Molecular Biology...

...dpascual@montana.edu.

Study 2: B7 costimulatory molecules play a role in mediating systemic and mucosal antibody responses to attenuated Salmonella enterica serovar Typhimurium and its cloned antigen.

"The purpose of the present study was to evaluate the ability of an attenuated Salmonella enterica serovar Typhimurium vaccine strain to up-regulate B7-1 and B7-2 on antigen-presenting cells and to examine the functional roles these costimulatory molecules play in mediating immune responses to Salmonella and to an expressed cloned antigen, the saliva-binding region (SBR) of antigen I/II. In vitro stimulation of B cells (B220+), macrophages (CD11b+), and dendritic cells (CD11c+) with S. enterica serovar Typhimurium induced an up-regulation of B7-2 and, especially, B7-1 expression," scientists in the ...

...type and B7-1, B7-2, and B7-1/2 knockout (KO) mice following intranasal immunization with the Salmonella expressing the cloned SBR," said Carlos A. Garcia and colleagues at the...

...Birmingham "Differential requirements for B7-1 and B7-2 were observed upon primary and secondary immunizations. Compared to wild-type controls, B7-1 and B7-2 KO mice had reduced mucosal and systemic anti- Salmonella antibody responses after a single immunization, while only B7-1 KO mice exhibited suppressed anti- Salmonella antibody responses following the second immunization."

"Mucosal and systemic antibody responses to SBR were reduced following the primary immunization, whereas a compensatory role for either B7-1 or B7-2 was observed after the second immunization," reported Garcia and his collaborators. "B7-1/2 double KO mice failed to induce detectable levels of mucosal or systemic IgA or IgG antibody responses to either Salmonella or SBR. These findings demonstrate... B7-1 and B7-2 can play distinct as well as redundant roles for mediating mucosal and systemic antibody responses, which are likely dependent upon the nature of the antigen."

Garcia and his coauthors published their study in Infection and Immunity (Role of B7 costimulatory molecules in mediating systemic and mucosal antibody responses to attenuated Salmonella enterica serovar Typhimurium and its cloned antigen. Infect Immun, 2004; 72(10):5824-5831).

For additional information, contact Suzanne M. Mchalek, Department of Microbiology...

...BBRB 285-5, Birmingham AL 35294-2170, USA. E-mail: suemich@ab.edu.

Study 3: Mucosal immunization with purified flagellin from Salmonella induces systemic and mucosal immune responses in mice.

According to a study from Sweden, "This study investigated the immune response elicited in C3H/HeJ mice after oral, parenteral and nasal immunization with purified flagellin from Salmonella enterica serovar Enteritidis alone or conjugated to starch microparticles as adjuvant or together with the uptake-enhancer recombinant cholera toxin B-subunit (rCTB). Systemic (IgM/IgG, IgA, IgG2a, IgG2b, IgG1) and local (s-IgA) humoral immune responses in the mice were analyzed using enzyme-linked immunosorbent assays (ELISA). Primed splenocytes were also stimulated in vitro with flagellin and the supernatants analyzed for cytokine production. Finally, immunized mice were challenged orally with live Salmonella..."

"A high flagellin-specific IgM/IgG response was seen in

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all groups, especially in mice immunized nasally with flagellin plus rCTB or subcutaneously, but a strong systemic antibody response was also induced when free antigen was given orally," stated Lena Strindell and colleagues at Uppsala University. "Intranasal or subcutaneous immunization of mice with flagellin plus rCTB or oral immunization with flagellin plus microparticles resulted in a significantly greater mucosal response (higher s-IgA titers in feces) than seen in the control group ( $p < 0.05$ ). The mucosal IgA responses were significantly correlated with the serum IgA titers."

"The subclass profile in serum revealed a mixed Th1/Th2-type response, with a predominance of Th1-type, as indicated by the subclass ratio (IgG1/IgG2a + IgG2b)," reported the scientists. "The splenocytes stimulated in vitro produced interferon (IFN)-gamma, at levels, which increased with time. The group immunized with flagellin plus rCTB subcutaneously had a relatively higher IFN-gamma response than the other groups. Interleukin (IL)-2 was also produced, especially in mice immunized nasally or subcutaneously with flagellin conjugated to microparticles. However, neither IL-4 nor IL-5 was produced in any of the groups."

"After oral challenge with live serovar Enteritidis, the groups immunized orally or nasally with free flagellin had significantly lower degree of infection than the control group ( $p < 0.05$ )," concluded the investigators.

Strindell and associates published the results of their research in Vaccine (Mucosal immunization with purified flagellin from Salmonella induces systemic and mucosal immune responses in C3H/HeJ mice. Vaccine, 2004;22(27-28):3797-3808).

For additional information, contact Ingvar Sjöholm, Department of Pharmacy...

...uu.se.

The information in this article comes under the major subject areas of Salmonella Vaccine, Vaccine Development, Food-borne illness, Mucosal Immunization, Proteomics, Immunology, and Immunotherapy.

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DESCRIPTORS: Food-borne illness; Immunization; Immunology  
; Montana State University; Mucosal  
Immunization; Proteomics; Salmonella Vaccine  
; Salmonella Vaccines; Therapy; Vaccine  
Development; and Immunotherapy; All News;  
Professional News

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0000192937 (USE FORMAT 7 OR 9 FOR FULLTEXT)  
Recent findings in salmonella vaccines described  
Immunotherapy Weekly, February 16, 2005, p.217

DOCUMENT TYPE: Expanded Reporting LANGUAGE: English  
RECORD TYPE: FULLTEXT  
WORD COUNT: 986

...TEXT: advances have been reported from Germany, Sweden and Bulgaria.  
Study 1: An attenuated Salmonella live vaccine expressing  
Qpr F-Qpr I from Pseudomonas aeruginosa exhibited enhanced

immunogenicity in the murine airway mucosa.

"We constructed an oral live vaccine based on the attenuated *aeruginosa* mutant *Salmonella enterica* serovar Typhimurium strain SL3261 expressing outer membrane proteins F and I (OprF-OprI) from *Pseudomonas aeruginosa* and...

...in vivo inducible protein expression with the P-pacC promoter showed good infection rates and immunogenicity but failed to engender detectable antibodies in the lung. However, a systemic booster vaccination following an oral primary immunization yielded high immunoglobulin A (IgA) and IgG antibody levels in both upper and lower airways superior to conventional systemic or mucosal booster vaccination alone," scientists writing in the journal *Infection and Immunity* report.

"In addition, the proportion of IgG1 and IgG2a antibodies suggested that the systemic booster does not alter the more Th1-like type of response induced by the oral *Salmonella* primary vaccination," said Heinz Arnold at Hannover Medical School and...

...in Germany. "We conclude that an oral primary systemic booster vaccination strategy with an appropriate mucosal vector may be advantageous in diseases with the risk of *P. aeruginosa* airway infection, such as cystic fibrosis."

Arnold and associates published their study in *Infection and Immunity* (Enhanced immunogenicity in the murine airway mucosa with an attenuated *Salmonella* live vaccine expressing OprF-OprI from *Pseudomonas aeruginosa*. *Infect Immun*, 2004;72(11):6546-6553).

Additional information can be obtained by contacting Ulrich Baumann, Department...

...Medical School, D-30623 Hannover, Germany. E-mail: baumann.ulrich@mh-hannover.de.

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response than the other groups. Interleukin (IL)-2 was also produced, especially in mice immunized nasally or subcutaneously with flagellin conjugated to microparticles. However, neither IL-4 nor IL-5 was produced in any of the groups."

"After oral challenge with live serovar Enteritidis, the groups immunized orally or nasally with free flagellin had significantly lower degree of infection than the control group ( $p < 0.05$ )," concluded the investigators.

Strindellius and associates published the results of their research in Vaccine (Mucosal immunization with purified flagellin from Salmonella induces systemic and mucosal immune responses in C3H/HeJ mice. Vaccine, 2004;22(27-28):3797-3808).

For additional information, contact Ingvar Sjöholm Department of Pharmacy...

...H antigens protected mice against intranasal challenge with Salmonella enterica serotype Enteritidis.

"Protective properties of immunoglobulin A (IgA) monoclonal antibodies (MAbs) directed against O and H antigens of Salmonella enterica serotype...

...1 hour before i.n. challenge did not prevent infection, and mice developed rapid inflammatory response in the lower respiratory tract," researchers in Bulgaria report.

The passive systemic immunization was partially protective and a single intravenous (i.v.) injection of both O and H...

...acad.bg.

The information in this article comes under the major subject areas of Salmonella Vaccine, Vaccine Development, Food-Borne Illness, Monoclonal Antibodies, Immunology, and Immunotherapy.

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DESCRIPTORS: Hannover Medical School; All News; Professional News; Immunology; Immunotherapy

30/3, K/33 (Item 6 from file: 135)  
DIALOG(R) File 135: NewsRx Weekly Reports  
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0000146316 (USE FORMAT 7 OR 9 FOR FULLTEXT)  
Factors affecting immune responses to Salmonella vaccine reported  
Immunotherapy Weekly, July 7, 2004, p.174

DOCUMENT TYPE: Expanded Reporting LANGUAGE: English  
RECORD TYPE: FULLTEXT  
WORD COUNT: 535

Factors affecting immune responses to Salmonella vaccine reported

TEXT: Scientists outline the host and bacterial factors affecting induction of immune responses to flagellin expressed by attenuated Salmonella vaccine strains in a recent issue of Infection and Immunity.

"Previous observations demonstrated that the delivery of recombinant Salmonella enterica serovar Dublin strains to mice via mucosal routes did not efficiently activate systemic and secreted antibody responses to

either type d flagellin or genetically fused heterologous B-cell epitopes, thus reducing the usefulness of the protein as a carrier of epitopes for vaccine purposes. In this work, we investigated murine systemic and mucosal flagellin immunogenicity after oral immunization with attenuated Salmonella strains," scientists in Brazil report.

"The reduced anti-type d flagellin antibody responses in mice immunized via mucosal routes with three doses of flagellated S. enterica serovar Dublin strains were not caused by oral tolerance and could not be restored by co-administration of a mucosal adjuvant," said Maria Elisabete Sbroglio-Almeida and colleagues at Sao Paulo University. "The induction of antibody responses to Salmonella flagellins was shown to differ according to the genetic background, but not the haplotype, of the mouse lineage."

"Moreover, BALB/c mice orally immunized with S. enterica serovar Typhimurium strains developed anti-type i flagellin sera and secreted antibody responses, which indicated that the serovar of the Salmonella vaccine strain also affected flagellin immunogenicity," stated Sbroglio-Almeida and her collaborators. "Analyses of cytokine responses of BALB/c mice immunized with three oral doses of flagellated S. enterica serovar Dublin vaccine strains showed that, in spite of the lack of antibody responses, elevated type d flagellin-specific CD4-cell-activation-dependent gamma interferon (IFN-gamma) and interleukin-10 responses were elicited after the administration of the vaccine strains via either parenteral or mucosal routes."

The investigators reported, "Similar cytokine production patterns were detected to a T-cell heterologous epitope, derived from the CFA/I fimbriae of enterotoxigenic Escherichia coli (ETEC), in mice orally immunized with a Salmonella vaccine strain expressing hybrid flagella. These results indicate that the immunogenicities of Salmonella flagellins can differ significantly, depending on the murine host and on the bacterial vector used, and demonstrate that the induction of CD4-cell-activation-dependent IFN-gamma production represents a major immune response triggered by flagellin and in-frame fused heterologous T-cell epitopes after the oral administration of recombinant S. enterica serovar Dublin vaccine strains."

Sbroglio-Almeida and her coauthors published their study in Infection and Immunity (Host and bacterial factors affecting induction of immune responses to flagellin expressed by attenuated Salmonella vaccine strains. Infect Immunology, 2004; 72(5):2546-2555).

For additional information, contact Luis Carlos de Souza Ferreira, Division...

...E-mail: lcsf@sp.br.

The publisher's contact information for the journal Infection and Immunity is: American Society for Microbiology, 1752 N Street NW Washington, DC 20036-2904, USA.

The information in this article comes under the major subject areas of Salmonella Vaccine, Food-Borne Illness, Vaccine Development, Bacteriology, Biotechnology, Immunology, Mucosal Immunization, and Immunotherapy.

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DESCRIP TORS: Sao Paulo University; Immunology; Bacteriology;  
All News; Professional News; Immunotherapy  
SUBJECT HEADIN G: Salmonella Vaccine

DI ALCOG R) File 357: Derwent Biotech Res.  
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0408892 DBR Accession No.: 2006-22388  
Safety and immunogenicity of attenuated *Salmonella enterica* serovar  
Typhimurium delivering an HIV-1 Gag antigen via the *Salmonella*  
Type III secretion system - *Salmonella enterica* for use in HIV virus  
infection recombinant vaccine  
AUTHOR: KOTTON CN; LANKOVSKI AJ; SCOTT N; SI SUL D; CHEN LM; RASCHKE K;  
BORDEERS G; BOAZ M; SPENTZOU A; GALAN JE; HOHMANN EL  
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Hosp, Infect Dis Div, 55 Fruit St, GRU 504, Boston, MA 02114 USA  
JOURNAL: VACCINE (24, 37-39, 6216-6224) 2006  
ISSN: 0264-410X  
LANGUAGE: English

Safety and immunogenicity of attenuated *Salmonella enterica* serovar  
Typhimurium delivering an HIV-1 Gag antigen via the *Salmonella*  
Type III secretion system - *Salmonella enterica* for use in HIV virus  
infection recombinant vaccine  
ABSTRACT: AUTHOR ABSTRACT - Background: CKS257 (*Salmonella*  
typhimurium SL1344 Delta phoP/phoQ Delta aroA Delta asd Delta  
strA/strB pSB2131) is a live oral vaccine vector expressing HIV  
Gag. Methods: HIV Gag was expressed as a fusion protein of a...

... 1 x 10(10) CFU of CKS257 and were monitored for clinical events,  
shedding and immune responses. Results: Adverse events were mild  
except at the highest dose. Volunteers shed the organism...  
... 1 days (range 0-13 days). Eighty-three percent (15/18) of subjects had a  
mucosal immune response to *Salmonella* LPS and  
flagella by IgA ELISPOT assay. Seventy-two percent (13/18) of  
subjects seroconverted to *Salmonella* antigens. No volunteer had a  
response to recombinant Gag as measured by serology, IgA ELISPOT,  
or immediate ex vivo gamma-interferon ELISPOT response to Gag  
peptide pools. Two volunteers responded to Gag peptides by IL-2  
ELISPOT, and 4 of 10 volunteers receiving andgt;= 5 x 10(8) CFU had a  
response to HIV peptides in a cultured gamma-interferon ELISPOT  
assay. Conclusions: Although immunogenicity of the HIV antigen  
needs augmentation, the attenuated *Salmonella* strain proved to be an  
excellent platform for vaccine development. (c) 2006 Elsevier  
Ltd. All rights reserved. (9 pages)  
DESCRIPTORS: ... HIV virus Gag antigen, SopE protein fusion gene transfer,  
expression in *Salmonella enterica*, human patient immunization,  
Western blot hybridization, appl. HIV virus infection recombinant  
vaccine bacterium virus AIDS leuko virus retro virus lenti virus  
protein sequence (25, 42)

30/3, K/35 (Item 2 from file: 357)  
DI ALCOG R) File 357: Derwent Biotech Res.  
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0377181 DBR Accession No.: 2005-22887 PATENT  
Mucosal vaccine adjuvants for preventing infectious diseases,  
anticancer and for contraception, comprises bacterial flagellins,  
as active component - bacterium flagellin and gene substitution  
for vaccine and disease therapy or prevention  
AUTHOR: RHEE J H; LEE S E; KIM S Y  
PATENT ASSIGNEE: UNIV CHONNAM NAT. 2005  
PATENT NUMBER: WO 200570455 PATENT DATE: 20050804 WPI ACCESSION NO.:  
Page 72



2005-542230 (200555)

PRIORITY APPLIC. NO.: KR 1974 APPLIC. DATE: 20040112

NATIONAL APPLIC. NO.: WO 2005KR103 APPLIC. DATE: 20050112

LANGUAGE: English

Mucosal vaccine adjuvants for preventing infectious diseases, anticancer and for contraception, comprises bacterial flagellins, as active component - bacterium flagellin and gene substitution for vaccine and disease therapy or prevention

ABSTRACT: DERIVATIVES ABSTRACT: NOVELTY - Mucosal vaccine adjuvants

(I), comprises bacterial flagellins, as an active component.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following: (1) producing (M) immunogen having adjuvanticity by flagellin, involves substituting the genes encoding protein antigen epitopes for the genes between the N-terminal...

... 377 and FlaE of amino acid sequence 276-375 among the structural components of *Vibrio vulnificus* set out in SEQ ID No. 1-12; and

(2) mucosal vaccine adjuvants (II), comprising immunogens prepared by (M), as an active component.

BIO TECHNOLOGY - Preferred Adjuvant: In (I), the flagellins are originated from *V. vulnificus*, *Salmonella typhimurium*, *Listeria monocytogenes*. The flagellins are chosen from flagellin proteins of *V. vulnificus* having SEQ ID No. 2, 4, 6, 8, 10 or 12, encoded by FlaA, FlaB...

... 5, 7, 9 or 11, respectively. In (II), the adjuvants are for the anti-toxin vaccine against tetanus toxoid and so on, the live attenuated or killed vaccines against cholera, typhoid fever, the anti-viral vaccine against influenza, severe acute respiratory syndrome, the anti-cancer vaccines against uterine cervical cancer, the anti-sperm contraceptive vaccine or the recombinant protein or peptide vaccine. Preferred Method: In (M), the protein antigen epitopes are tetanus toxoid, immunogenic epitopes of influenza virus, immunogenic epitopes of human papilloma virus that induces uterine cervical cancer, pneumococcal antigen PspA or sperm ACTIVITY - Antimicrobial; Cytostatic; Contraceptive. MECHANISM OF ACTION -

Vaccine. The antigen specific systemic immune response and mucosal immune adjuvanticity of the recombinant flagellin was carried out as follows. Seven-week-old Balb/c mice were intranasally immunized 3 times with phosphate buffered saline (PBS), tetanus toxoid or with combinations of 3 of tetanus toxoid (TT) and of FlaB of *V. vulnificus* (Vv) at 7 day interval. Seven days after the last immunization, saliva, vaginal wash, and serum samples were collected to assess TT-specific systemic immune responses and mucosal immune responses. These responses were measured by enzyme linked immunosorbent assay (ELISA). The mice that were vaccinated 3 times before were observed for 7 days...

...of 200 folds of lethal doses of (TT). Results indicated that the antigen specific systemic immune response and mucosal immune response was higher in the group of TT+Vv-FlaB than that in the group of...

...preventing infectious diseases, cancer, and also useful in contraception etc. ADMINISTRATION - (I) is administered by mucosal route (claimed), or by subcutaneous, intravenous, intramuscular or oral route. No dosage given. EXAMPLE - No...

DESCRIPTIONS: *Vibrio vulnificus*, *Salmonella typhimurium*, *Listeria monocytogenes* flagellin, FlaA, FlaB, FlaF, FlaC, FlaD, FlaE gene substitution, human papilloma virus, influenza virus, severe-acute-respiratory-syndrome virus, antitumor vaccine,



interleukin-2 (IL-2), IL-6, IL-7, IL-18, type I...

... chosen from water (H<sub>2</sub>O), aqueous salt solution and buffer solution. ACTIVITY - Cytostatic; Antiinflammatory; Antimicrobial; Antirheumatic; Immunosuppressive; Antiallergic; Vasotropic. MECHANISM OF ACTION - Vaccine. The effects of various AVE3-based formulations on the generation of an immune response in mice using a TRP-2 peptide (Ser-Val-Tyr-Asp-Phe-Phe-Val-Trp-Leu) as antigenic model peptide were analyzed. Mice (C57BL/6) were immunized by a single injection into the hind footpad. After 4 days mice were sacrificed, the ...

... were cultured for 6-7 days in the presence of interleukin-2. Cells were then stimulated with the antigenic peptide (TRP-2) or an irrelevant peptide (OVA peptide; Ser-Ile-Ile...

... CD8+ cells at a concentration of 50-100 micrograms/animal. Unencapsulated CpG gave a strong immune-response at concentrations of 2.5-5 nmol/animal. USE - (I) and (II) are useful for ...

... the prevention or therapy of proliferative diseases, infectious diseases, vascular diseases, rheumatoid diseases, inflammatory diseases, immune diseases, and allergies. The proliferative disease is chosen from carcinomas of the gastrointestinal or colorectal tract, liver, pancreas, kidney, bladder, prostate, endometrium, ovary, testes, melanoma, dysplastic oral mucosa, invasive oral cancers, small cell and non-small cell lung carcinomas, hormone-dependent breast cancers...

... fibromas, histiocytosis, chronic inflammatory proliferative diseases, vascular proliferative diseases and virus-induced proliferative diseases. The adjuvant and/or a cytokine is (are) administered prior, simultaneously or after administration of (I) or...

DESCRIPTIONS: recombinant vaccine, nucleic acid vaccine, liposome vector-mediated tumor-associated antigen, gene expression, adjuvant, appl., proliferative disease, infectious disease, vascular disease, rheumatoid disease, inflammatory disease, immune disease, allergy, gastrointestinal carcinoma, colorectal carcinoma, liver tumor, pancreas carcinoma, kidney carcinoma, bladder carcinoma, prostate carcinoma, endometrium carcinoma, ovary carcinoma, testes carcinoma, melanoma, dysplastic oral mucosa carcinoma, invasive oral cancer, small cell lung carcinoma, non-small cell lung carcinoma, hormone-dependent...

...disease, virus-induced proliferative disease, therapy, gene therapy, lipofection transfection tumor cytostatic antiinflammatory antimicrobial antirheumatic immunosuppressive antiallergic vasotropic (24, 34)

30/3, K/37 (Item 4 from file: 357)  
DIALCOG File 357: Derwent Biotech Res.  
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0344928 DBR Accession No.: 2004-17220  
Host and bacterial factors affecting induction of immune responses to flagellin expressed by attenuated *Salmonella* vaccine strains - recombinant bacterium and bacterium flagellin for use in vaccine

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CORPORATE SOURCE: Ferreira LCS, Univ Sao Paulo, Dept Microbiol., Inst  
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Brazil

JOURNAL: INFECTION AND IMMUNITY (72, 5, 2546-2555) 2004

ISSN: 0019-9567

LANGUAGE: English

Host and bacterial factors affecting induction of immune responses to  
flagellin expressed by attenuated *Salmonella* vaccine  
strains - recombinant bacterium and bacterium flagellin for use  
in vaccine

... ABSTRACT: observations demonstrated that the delivery of recombinant  
*Salmonella* enterica serovar Dublin strains to mice via mucosal  
routes did not efficiently activate systemic and secreted antibody  
responses to either type d flagellin or genetically fused  
heterologous B-cell epitopes, thus reducing the usefulness of the  
protein as a carrier of epitopes for vaccine purposes. In this  
work, we investigated murine systemic and mucosal flagellin  
immunogenicity after oral immunization with attenuated  
*Salmonella* strains. The reduced anti-type d flagellin antibody  
responses in mice immunized via mucosal routes with three  
doses of flagellated *S. enterica* serovar Dublin strains were not  
caused by oral tolerance and could not be restored by coadministration  
of a mucosal adjuvant. The induction of antibody responses  
to *Salmonella* flagellins was shown to differ according to the  
genetic background, but not the haplotype, of the mouse lineage.  
Moreover, BALB/c mice orally immunized with *S. enterica* serovar  
Typhimurium strains developed anti-type i flagellin sera  
and secreted antibody responses, which indicated that the serovar of  
the *Salmonella* vaccine strain also affected flagellin  
immunogenicity. Analyses of cytokine responses of BALB/c mice  
immunized with three oral doses of flagellated *S. enterica*  
serovar Dublin vaccine strains showed that, in spite of the lack  
of antibody responses, elevated type d flagellin-specific  
CD4-cell-activation-dependent gamma interferon (IFN-gamma) and  
interleukin-10 responses were elicited after the administration of the  
vaccine strains via either parenteral or mucosal routes.  
Similar cytokine production patterns were detected to a T-cell  
heterologous epitope, derived from the OFA/I fimbriae of  
enterotoxigenic *Escherichia coli* (ETEC), in mice orally immunized  
with a *Salmonella* vaccine strain expressing hybrid  
flagella. These results indicate that the immunogenicities  
of *Salmonella* flagellins can differ significantly, depending on  
the murine host and on the bacterial vector used, and demonstrate that  
the induction of CD4-cell-activation-dependent IFN-gamma production  
represents a major immune response triggered by  
flagellin and in-frame fused heterologous T-cell epitopes after  
the oral administration of recombinant *S. enterica* serovar Dublin  
vaccine strains. (10 pages)

DESCRIPTORS: vector plasmid pLS408-mediated gene transfer expression in  
attenuated *Salmonella* enterica recombinant vaccine,  
flagellin immunogenicity, mouse host, bacterium factor,  
appl. immune response induction bacterium protein mammal  
animal (23, 36)

30/3, K/38 (Item 1 from file: 457)

DIACOR File 457: The Lancet

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0000071045

\*\*USE FORMAT 7 OR 9 FOR FULL TEXT\*\*

The mechanisms and efficacy of probiotics in the prevention of *Clostridium*

difficile-associated diarrhoea

Parkes, Gareth C; Sanderson, Jeremy D; Whelan, Kevin  
The Lancet Infectious Diseases vol. 9, 4 PP: 237-44 Apr 2009  
DOCUMENT TYPE: PERIODICAL; General Information; Journal Article  
LANGUAGE: English RECORD TYPE: New; Fulltext  
LENGTH: 8 Pages  
WORD COUNT: 6602

# TEXT:

...by detecting toxin A or B, or both, in the stool using an enzyme linked immunosorbent assay.5 Tests that only detect toxin A can lead to a substantial rate of...show functional efficacy. With respect to the prevention of CDAD, these important functional characteristics include immune stimulation and the suppression of enteropathogenic colonisation, adhesion, and invasion.

Probiotics stimulate immune function in a number of ways. Cellular and animal models have demonstrated that probiotics can have a profoundly anti-inflammatory effect via the innate immune response42-46 and lamina propria dendritic cells.47-49 The host immune response to C difficile colonisation and toxin production is crucial in influencing disease severity.26,50...

...may suppress enteropathogenic colonisation of the lumen and subsequent adhesion and invasion of the gastrointestinal mucosa. For example, a number of in-vitro studies, mostly with Escherichia coli and Salmonella enterica serotype typhimurium (S typhimurium),54,55 have demonstrated that select probiotics inhibit enteropathogenic growth. Subsequent studies have demonstrated similar...

...of enteropathogens. For example, some lactobacilli and bifidobacteria inhibit adhesion of E coli and S typhimurium to human enterocyte cell lines57,60 and mucous.61 This may occur through steric hindrance of pathogen adhesion sites or biochemical hindrance through...

...of CDAD. These trials can be divided into those assessing the efficacy of probiotics as adjuvant therapy in conjunction with antibiotics to prevent disease recurrence (secondary prophylaxis), and those assessing the efficacy of probiotic strains for any clinical indication is problematic. The species-specific and immunomodulatory effects of the strains limits the statistical aggregation of trials of different probiotics, which should...

...17% in the placebo group (p<0.01). However, the exclusion criteria included severe illness, immunosuppression, and high risk antibiotics, leading to 92% of screened patients being excluded from the study. Therefore...

...of prevention and treatment strategies. There is renewed interest in novel antibiotics, the use of immunoglobulins, and the development of sporicidal cleaning agents. Probiotics have the potential to complement these strategies...

...resist C difficile colonisation and toxin release highlights this potential. Probiotic bacteria can have profound immunological and metabolic effects within the gastrointestinal tract. Animal and cell culture studies have demonstrated that some probiotic strains can stimulate immune function, resist C difficile colonisation, and hydrolyse C difficile toxin. They may also have a...

...applied to other probiotics or other patient groups. In view of the differences in the immunological and antipathogenic effects between different probiotics, clinicians are advised to use only those probiotic strains...

...in vivo human studies investigating the mechanism of action of probiotics against CDAD. Microbiological and immunological analysis of stool and colonic mucosa of patients undergoing probiotic trials might improve our understanding of the mechanisms underlying their efficacy... of guidelines has divided the risk factors for adverse events following probiotic use into major (immune compromise, premature infant) and minor (central venous catheter, impaired intestinal barrier function, administration via jejunoscopy...

...that confer a health benefit.97 For example, fructooligosaccharides increase the concentration of faecal associated and mucosa-associated bifidobacteria in the human colon98,99 and have been shown to substantially reduce disease...

SI DEBAR:

CITED REFERENCES:

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THIS IS THE FULL-TEXT.

30/3, K/39 (Item 2 fromfile: 457)  
DI ALCO (R) File 457: The Lancet  
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0000063527

\*\*USE FORMAT 7 OR 9 FOR FULL TEXT\*\*

Necrotising enterocolitis  
Lin, Patricia W, Stoll, Barbara J  
The Lancet vol. 368, 9543 PP: 1271-83 Oct 7-Oct 13, 2006  
DOCUMENT TYPE: PERIODICAL; Feature; Journal Article LANGUAGE: English  
RECORD TYPE: New; Fulltext  
LENGTH: 13 Pages  
WORD COUNT: 11056

TEXT:

...of key functions, in particular gastrointestinal motility, digestive  
ability, circulatory regulation, intestinal barrier function, and  
immune defence. Other potential contributing factors include  
hypoxic-ischaemic injury, feeding with formula milk, and colonisation...

...more useful.59

Immature regulation of intestinal circulation might lead to intestinal  
hypoxia-ischaemia in response to feeding or to the presence of  
abnormal bacteria. Some studies indicate that immature animals have altered  
circulatory regulation in response to ischaemia or haemorrhage;  
others suggest that they do not.60,61 Reduced endothelial production...  
specialised enterocytes secrete gram quantities of mucins, forming a thick  
protective layer over the intestinal mucosa. This mucus layer hampers  
direct microbial epithelial binding, aggregates adherent bacteria, and  
enhances bacterial removal.72...

...the intestinal epithelial barrier, and increasing susceptibility to  
injury by pathogenic or even non-pathogenic stimuli (figure 2).

Another aspect of the intestinal epithelial barrier that may not be  
functioning correctly...

...the defensins (alpha and beta) and cathelicidins.74,76 Paneth cells  
secrete alpha-defensins in response to microbial stimuli.76,77  
Intestinal epithelial cells mainly secrete beta-defensins, and some cells  
can upregulate expression of defensins in response to  
pro-inflammatory stimuli.74,78,79 These antimicrobial peptides have  
bioactivity against a wide range of microbes, including...

...shown that some antimicrobial peptides have a pro-inflammatory role (in  
secreting cytokines and recruiting immune cells) and Q- secretory  
activity (presumably in flushing the crypt of unwanted pathogens and

toxins). 82-85 A better understanding of the way defensin and cathelicidin modulate host immune defences in vivo should contribute to understanding the pathophysiology of necrotising enterocolitis.

Studies in mice...

...pathogenesis, especially if abnormal colonisation occurs. Little is known about the functional status of innate immune signalling pathways during prenatal and postnatal development in vivo, but intestinal colonisation might affect maturation...Likelihood of exposure to antibiotics on admission to NICUs.112 Furthermore, reports indicate that pathogenic stimuli, including *Salmonella* and *Escherichia coli*, produce exaggerated proinflammatory responses in immature intestinal epithelial cells.113...

...epithelial cells upregulate expression of a PRR known as toll-like receptor 4 (TLR4) in response to stress-induced production of platelet activating factor (PAF); upregulation of TLR4 might explain how necrotising enterocolitis develops in this animal model.116

Immature intestinal innate immunity

A series of events probably induces the inflammatory response that ultimately causes the mucosal oedema, coagulation necrosis, and haemorrhage that characterise necrotising enterocolitis (figure 5).93,117 Inflammatory mediators...

...12, and IL-18).116,118-121 Inflammation is a tightly regulated and programmed host response that recruits leucocytes to aid in the defence against potential pathogens and in the initial response to damaged tissue. The inflammatory process begins when signals of potential danger induce local release...

...a key defence mechanism in the microbe-rich environment of the intestine. However, the inflammatory response results in collateral damage caused by the release of neutrophil-derived oxidants and proteases. These molecules...

...access for micro-organisms that cannot normally breach the epithelial barrier. These organisms could further stimulate pro-inflammatory activation and tissue damage. Some invitro studies suggest that immature intestinal cells seem to have a propensity for exaggerated inflammatory responses to pathogenic stimuli,113,114 and researchers postulate that developmentally deficient expression of the NF-kappaB inhibitor IkkappaB might allow greater NF-kappaB activity. In this model, an exaggerated inflammatory response (which might be caused by immature or abnormal PRR signalling) could cause increased cellular inflammation...

...intestinal pro-inflammatory responses.116 They hypothesise that abnormal upregulation of intestinal epithelial TLR4 in response to stress (hypoxia and formula feeding) causes increased inflammatory signalling in response to normal bacterial colonisation.116 But this study was conducted in an animal model of...

...with gut enterocytes that are conditionally null for NF-kappaB activation, intestinal apoptosis ensues in response to transient hypoxia.123 Thus, developmental immaturity of the inflammatory response could increase susceptibility to apoptosis when cells are challenged by environmental stress. Host health is...

...between exaggerated pro-inflammatory activation (causing tissue injury and clinical sequelae) and insufficient inflammation (leaving mucosa vulnerable to uncontrolled bacterial growth, poised to self-destruct, or both).102 In a rat...

...PRRs have been shown to sense invading bacteria and activate gene transcription pathways that regulate immune and inflammatory



responses.125 In a recent clinical study, VLBW infants with mutations in a ... development and defence, and that nonnutritive dietary substances, such as epidermal growth factor and polyanines, stimulate intestinal epithelial growth.158, 159 Furthermore, some nutrients (such as glutamine, arginine, and omega-3...

...infants fed control formula.168 Furthermore, prebiotic treatment may have a positive effect on host immune function.169 Because prebiotic supplements do not contain live micro-organisms, they carry less risk...

...probiotics (heat-killed commensals) or bio-available toll-like receptor ligands could potentially induce beneficial TLR-mediated protective effects without carrying the infectious risk of probiotic therapies. But the neonatal epithelia...

SI DEBAR:

CAPTIONS:

...nucleus and induces transcription of pro inflammatory and antiapoptotic genes.

Figure 5: Immature intestinal innate immunity

Figure 6: Suggested management of necrotising enterocolitis

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New genes in inflammatory bowel disease: lessons for complex diseases?

Gaya, Daniel R; Russell, Richard K; Nimmo, Elaine R; Satsangi, Jack

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TEXT:

...data that have been generated since the discovery of the CARD15 (NOD2) gene in 2001.

Stimulated by epidemiological findings,1 suggesting a substantial genetic contribution to disease susceptibility in inflammatory bowel...

...is important in the pathogenesis of Crohn's disease has refocused attention on the innate immune response and the interaction between genetic factors and bacterial flora, or pathogen-associated molecular patterns.

Evidence...

...figure 2, the clinical spectrum is likely to be the result of interactions between environmental stimuli (eg, smoking), susceptibility genes (which predispose to the development of bowel inflammation), and modifier genes...bowel disease strongly induce expression of defensins in vitro.84 Thus, upregulation of the innate immune response might be a therapeutic approach in inflammatory bowel disease. CARD15 seems to act as part...

...now available. Overexpression of CARD15 in intestinal epithelial cells results in reduced survival of Salmonella typhimurium.86 Wildtype and CARD15-deficient mice show no difference in protective response to intravenous and intraperitoneal listeria infection. However, in the knockout mouse model, loss of response occurs to administration of intragastric listeria accompanied by substantial infection.71 The fact that the...

...a crucial role in the elimination of intracellular pathogens in epithelial cells at the gastrointestinal mucosal barrier.

CARD15 mutation: gain or loss of function?

One paradox has become central to understanding...

...s disease is characterised by increased NFkappaB activation with downstream effects on cytokine production and immunoregulation.87,90 More recent data involving genetically engineered models and ex-vivo organ culture from...

... showed that the CARD15 protein can act as an important regulator of NF- $\kappa$ B activation in response to the toll-like receptor (TLR) 2 activation system.69 Located at the cell surface, this receptor is activated by peptidoglycan...

...a mouse knock-in model leads to a gain of function with raised NF- $\kappa$ B in response to muramyl dipeptide in macrophages from the mutants. This result is consistent with the in...

...used in the experiments, use of mouse or human cells, and use of peripheral or mucosal lymphocytes. Furthermore, several other components of the innate immune pathway interact with and modify CARD15 function: GRIM-19, NEMO, and RIPK2 are all involved...

...95

Pattern recognition receptor interactions

Further interactions between CARD-like molecules and members of the TLR family have been reported lately. These receptors are the cell-surface receptor equivalent of CARD15...

...molecular patterns at the cell surface. Several studies have shown interplay between CARD15 activation and TLR signalling pathways in human cells.74, 92, 93, 96-98 Again, these interactions are not...

...anti-inflammatory cytokines has been shown in Crohn's disease patients with CARD15 mutations, after stimulation with a TLR2 ligand.73

Although some data are conflicting, 99, 100 most lend support to the theory that CARD15 mutations impair signalling in the innate immune response to pathogen-associated molecular patterns, leading to less efficient clearing by the intestinal epithelium and subsequent...

...inflammation. Thus, the CARD15 discovery has renewed impetus to investigate the importance of the innate immune response and of bacterial pathogen-associated molecular peptides and specific pathogens themselves.

IBD3: the major histocompatibility...

...lead to large interindividual differences in the capacity to respond to antigens in the acquired immune system. Before the application of genome-wide scanning, the MHC was the candidate region that...widely established, although meta-analyses do provide consistent findings. Orchard and colleagues<sup>110, 111</sup> suggested distinct immunogenetic associations in type 1 arthropathy (large joint-oligoarthropathy) that flares during active exacerbations of inflammatory...myeloid cells accounts for the disease phenotype. Importantly, these mice have normal viability, fertility, and immunology as well as normal biochemical indices.<sup>133, 134</sup> Several other animal models of colitis have...

...expression of ABCB1) are all strongly downregulated in unaffected colonic tissue.<sup>147</sup> Functional data on mucosal P-glycoprotein 170 activity in people with and without inflammatory bowel disease are therefore eagerly...that gender may well represent a confounding factor in many of the subsequent datasets.

Innate immunity

Candidate gene analysis has lately focused on the innate part of the immune system, which senses the intraluminal milieu non-specifically and rapidly.

TLR4

The TLR class of receptors have a key role in maintenance of epithelial homeostasis in the gut: mice deficient in TLR signalling are more susceptible than wildtype mice to colitis induced by dextran sodium sulphate or...

...prevent the development of colitis in two independent mouse models, again suggesting that this innate immune receptor is central to the pathogenesis of inflammatory bowel disease.167

#### TLR5

TLR5 specifically recognises the pathogen-associated molecular pattern flagellin, a common antigen present on most motile bacteria in the gut.168,169 Lodes and...

...identify specific bacterial antigens that drive experimental inflammatory bowel disease; they recorded a strong serological response to flagellin in several animal models of colitis. The same researchers induced colitis by transferring flagellin-specific T cells to immunodeficient animals. Two studies have indirectly implicated flagellin sensing by TLR5 in the pathogenesis of Crohn's disease. First, synergism has been identified...

...stop) seems to protect against Crohn's disease and results in a substantial decrease in flagellin-specific IgA and IgG.171 Thus, these observations link a genetic defect in the innate immune system with alterations in the acquired immune response; they suggest that pharmacological blockade of TLR5 has potential in the treatment of Crohn's...

...Functional data from two groups using human cells have now revealed synergism between CARD4 and TLR signalling in cytokine activation,178,179 possibly through R1PK2, which is a common link in...

...suggested that the CARD4 agonist gamma-D-glutamyl mesodiaminopimelic acid does not induce a cytokine response in peripheral-blood mononuclear cells from Crohn's disease patients with CARD4 frameshift mutations, but...

...many genome-wide scans have also been identified in other complex disorders involving the inflammatory response. These loci include the HLA region on chromosome 6 and the CCTN region of chromosome...factors and bacteria within the gut. Whether through defective intracellular (CARD4, CARD15) or cell surface (TLR) bacterial recognition, antigen processing (HLA molecules), protection against xenobiotics (ABCB1), or a breakdown in epithelial...

...that inflammatory bowel disease results from a genetic predisposition to abnormal interaction with an environmental stimulus-most probably part of the normal luminal bacterial flora-which in turn leads to excessive immune activation and chronic inflammation. The discovery of the importance of germine variation of the CARD15...

#### SI DEBAR: CAPTIONS:

...overlapping syndromes sharing some phenotypes, and additionally sharing some genetic and environmental susceptibility and modifying stimuli. However, some phenotypic features and environmental/ genetic factors are specific to one or other disorder...

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DI ALCG R/ File 457: The Lancet

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\*\*USE FORMAT 7 OR 9 FOR FULL TEXT\*\*

Typhoid and paratyphoid fever

Bhan, M K; Bahl, Rajiv; Bhatnagar, Shrinjini

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#### ABSTRACT:

...reduced susceptibility to fluoroquinolones is of great concern. We discuss the occurrence of poor clinical response to fluoroquinolones despite disc sensitivity. Developments are being made in our understanding of the molecular...

...for selection of antimicrobials in varying clinical situations. The importance of safe water, sanitation, and immunisation in the presence of increasing antibiotic resistance is paramount. Routine immunisation of school-age children with Vi or Ty21a vaccine is recommended for countries endemic for typhoid. Vi vaccine should be used for 2-5 year-old children in highly endemic settings.

#### TEXT:

...reduced susceptibility to fluoroquinolones is of great concern. We discuss the occurrence of poor clinical response to fluoroquinolones despite disc sensitivity. Developments are being made in our understanding of the molecular...

...for selection of antimicrobials in varying clinical situations. The importance of safe water, sanitation, and immunisation in the presence of increasing antibiotic resistance is paramount. Routine immunisation of school-age children with Vi or Ty21a vaccine is recommended for countries endemic for typhoid. Vi vaccine should be used for 2-5 year-old children in highly endemic settings.

Typhoid fever...

...a few countries, with only one study providing data from Africa. Placebo groups from typhoid vaccine trials were included, and vaccine trials are usually done in areas with high disease burden. Some assumptions used also merit...or frameshifts, 145 of them are present as active genes in *S. typhimurium*. Significantly, *S. typhimurium* causes a different disease in people, and has a wider host range than *S. typhi*...

...*S. typhi*, 59

Pathogenesis

*S. typhi*, unlike *S. typhimurium*, avoids triggering of an early inflammatory response in the gut of the human host, using a stealth approach to allow colonisation of...



...typhoid fever pathogenesis we provide is based largely on the murine model in which *S typhi* murium causes a systemic infection similar to typhoid.

*S typhi* probably invades the gut mucosa in the terminal ileum through specialised antigen-sampling cells, known as M cells, which overlie ...

...61 through enterocytes, or via a paracellular route.62 The bacteria adhere to the intestinal mucosa in the terminal ileum through interaction with an epithelial receptor, the cystic fibrosis transmembrane conductance...seen in typhoid carrier state, has been proposed.2 Differences in mouse susceptibility to *S typhi* murium have been linked to the particular allele of the *Nramp1* gene expressed on their macrophages ...

...infection. Mice expressing the wildtype *Nramp1* allele did not die after oral inoculation with *S typhi* murium but became uniformly persistently infected as did chronic typhoid carriers.76 *Salmonella* persisted in small...

...in the macrophages of mesenteric lymph nodes or spleen (or both), despite a robust antibody response. Reactivation of intracellular salmonella and systemic spread could be accomplished by administering antibodies to neutralise...

...typhi.124

The Widal test identifies the agglutinating antibodies against the O (somatic) and H (flagellar) *S typhi* antigens, which appear a week to 10 days after disease onset. The sensitivity...is an obstacle to further development.134 DNA probes and PCR-based tests to detect flagellar genes135 are not routinely useful in developing countries, but they are of value in surveillance...

...previous exposure or vaccination, and other host factors such as HLA type, AIDS or other immune suppression, or antacid consumption. The commonest complications are gastrointestinal bleeding, intestinal perforation and typhoid encephalopathy...culture. Such short-term regimens are especially useful in control of epidemics. By contrast, the response of NAR isolates to such regimens is poor. Ofloxacin given for 7 days cured only...should be targeted for vaccination.

The old parenteral whole-cell typhoid-paratyphoid A and B vaccine was effective against both typhoid and paratyphoid fevers but has been largely discontinued because of...

...the other on whole-cell live attenuated bacteria, are currently licensed. A new Vi-conjugate vaccine is highly effective in children younger than 5 years but it has not been tested in infants. Currently, there is no licensed vaccine for paratyphoid fever.

Vi polysaccharide vaccine

This vaccine is licensed for use in individuals older than 2 years and is given in a single subcutaneous or intramuscular dose. The vaccine is moderately effective for about 3 years after vaccination (table 7).14,21,188,189...

...in South Africa still had protective levels of antibodies 10 years after vaccination.192 This vaccine has shown about 70% protective efficacy in a population vaccinated before or during an outbreak in China.189 The Vi vaccine can be given simultaneously with other vaccines relevant for international travellers such as yellow fever and hepatitis A.190,191,193

Ty21a vaccine

This live oral vaccine available in enteric-coated or liquid formulation is approved for use in people 6 years...

... 2 days apart. Antimicrobials should be avoided for 7 days before or after vaccination. The vaccine is moderately effective for up to about 3 years after vaccination (table 7).11-13...

...is recommended every 3 years in endemic areas and travellers should be revaccinated annually. Herd immunity was shown during field trials in Chile.11,13 The vaccine can be given simultaneously with other vaccines and with antimalarial prophylaxis.196

The effectiveness of...

...Ty21a has the advantage that it is given orally and therefore might be easier for immunising groups of children, as in schools. The Ty21a vaccine, especially the enteric-coated capsule formulation, is not licensed for use in 2-5 year-old children. Vi vaccine has a relative advantage that it can be used for these preschool children, in settings where typhoid fever is common in this age-group. The vaccine however, is not licensed for use in children younger than 2 years.

Post-marketing surveillance for typhoid fever vaccines from the Vaccine Adverse Effects Reporting System from 1990 to 2002 has shown rare reports of death, admission...

...or life-threatening illness.197 Unexpected frequently reported symptoms included dizziness and pruritis for Vi vaccine and fatigue and myalgia for Ty21a. Gastroenteritis for Ty21a and abdominal pain after Vi vaccine are previously recognised events.

Vi-conjugate vaccine

Vi-conjugate vaccine given to 2-5 year-old Vietnamese children had 91.1% protection against typhoid 27...titres after 46 months of vaccination, the researchers suggest a protective level of antibody to immunoglobulin G to be reduced from 7 to 3.52 ELISA units. This vaccine could be used for children younger than 2 years and be incorporated into the Expanded Programme on Immunization immunisation schedules.

Vaccines under development

Vaccines are under development based on outer membrane proteins known as...

...live oral vaccines (eg CVD 908-htrA and Ty2 candidate vaccines).199-201 A new vaccine against S paratyphi A composed of surface-O-specific polysaccharide conjugated with tetanus toxoid has proved safe and immunogenic.202 Live typhoid vaccines are being developed as a vector for immunisation against H pylori.203

Conclusion

Typhoid fever is an important public-health problem in south...

...not been reported, although full resistance in non-typhoid salmonella has emerged.204,205 Effective immunisation and non-vaccine based prevention strategies are available and are becoming more important in the face of increasing...

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30/3, K/42 (Item 5 from file: 457)

DI ALCO (R) File 457: The Lancet

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\*\*USE FORMAT 7 OR 9 FOR FULL TEXT\*\*

Unlocking the genome of the human typhoid bacillus

Wain, John; House, Deborah; Parkhill, Julian; Parry, Christopher; Dougan, Gordon

The Lancet Infectious Diseases vol. 2, 3 PP: 163-170 Mar 2002

DOCUMENT TYPE: PERIODICAL; General Information LANGUAGE: English

RECORD TYPE: New, Fulltext

LENGTH: 8 Pages

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TEXT:

...the whole-cell vaccines and were thus a significant improvement. A live attenuated oral typhoid vaccine, Ty21a, has also been in general use for some years. This vaccine has moderate efficacy in disease-endemic areas but requires several doses to achieve a reasonable... be present at the same site in even closely related bacteria (*Styphi* versus *Styphi* *murium* for example).

Another unexpected feature of the *Styphi* genome was the presence of more...

...biological consequences. 145 of the *Styphi* pseudogenes are present as active genes in *Styphi* *murium* and many are potentially involved in pathogenesis or encode proteins that are exported through the bacterial membranes and could be involved in immune recognition or pathogenesis. Significantly, *Styphi* *murium* causes a different disease in humans and has a wider host range compared with *S...*

...is summarised in figure 3. The number of publications on human typhoid that used modern immunological and molecular techniques is limited. Consequently, much of the detail of our perception of typhoid...

...on the inoculating dose of viable bacteria. After ingestion, *Styphi* pass through the intestinal mucosa, enter the mesenteric lymphoid system, and then pass into the bloodstream via the lymphatics. This...

...via the gall bladder.

*Styphi* are thought to invade the body through the gut mucosa in the terminal ileum possibly through specialised antigen-sampling cells, known as M cells, which *typhimurium* is not generally an invasive disease and is typically associated with gastroenteritis. Although diarrhoea can...

... studies with human cell lines have shown qualitative and quantitative differences in the epithelial-cell-response to S typhi and S typhimurium with regards to cytokine and chemokine secretion.22 Thus by avoiding the triggering of an early inflammatory response in the gut, S typhi could be seen to use a "stealth approach" to allow...

...A comparison of the genome sequence of S typhi with that recently published for S typhimurium LT224 identifies other smaller S typhi-specific gene clusters or individual genes. We will now... of S typhi could be clonal, studies from genome sizing<sup>34</sup> and variations in biotype and flagella antigen suggest that differences in the genetic repertoire of S typhi do occur.

Other differences...

...test is the Widal test, which detects agglutinating antibodies against the O (lipopolysaccharide) and H (flagella) antigens of S typhi. Although this test is widely used, it lacks sensitivity and/or... toilets was the cheapest way to reduce infection, but that vaccination with heatkilled whole-cell vaccine was more effective, especially in the short term. A combination of both measures was necessary...

SI DEBAR:

CITED REFERENCES:

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Section V: biomedical sciences.  
Georgia Journal of Science, 66, 1, 28(9)  
Spring,  
2008

PUBLICATION FORMAT: Magazine/Journal ISSN: 0147-9369 LANGUAGE: English

RECORD TYPE: Fulltext TARGET AUDIENCE: Academic

WORD COUNT: 5396 LINE COUNT: 00455

TEXT:

PROSTATE CANCER AND CONSTITUTIVE EXPRESSION OF IMMUNOSUPPRESSIVE CYTOKINES AND CHEMOKINES, Godwin A. Ananaba\* (1), K. Gordon (1), G. Ifere A. Campbell...

...Disease Control & Prevention, Atlanta, GA 30333. Cytokines and chemokines and their cognate receptors are essential immune effector molecules that are known to be involved in tumor progression. The specific cytokines and chemokines in particular are generally immunosuppressive and have been reported to be elevated in a large number of advanced tumors and...

...prostate tumor cell lines may explain a possible mechanism for them to negatively modulate the immune response and support their metastatic potential. Cytokines and chemokines may be used as potential diagnostic biomarkers for prostate cancer disease progression. In addition, an efficacious vaccine against prostate cancer will depend on its ability to inhibit the recruitment of known distinct...

THE DEVELOPMENT OF A PROPHYLACTIC VACCINE AGAINST CHLAMYDIA TRACHOMATIS GENITAL INFECTION\*\*, A. Campbell\*, E. Ekong (2), G. Ifere (1), T. Belay...

...is a prevalent bacterial sexually transmitted disease. Vaccinology strategies are attempting to produce an effective vaccine that would confer immunity against genital chlamydial infection. Our strategy is to develop of a vaccine scheme that utilizes a commensal bacteria as a live delivery vehicle of chlamydia antigens to the immune system. Lactobacilli are of the normal flora of the human genital and urinary tracts. We hypothesize that a vaccine utilizing lactobacilli as a live delivery vehicle will produce significant quantities of chlamydia antigen and induce mucosal, humoral and cell-mediated immune responses. In our laboratory, a plasmid construct DNA pGKOMP1 harboring the omp1 gene of C...

...construct and verified its orientation. The expression of plasmid pGKOMP1 in Lactobacillus constitutes a recombinant vaccine with the potential to produce an efficacious vaccine against C. trachomatis genital infection. Our vaccine scheme can be used for vaccinology efforts towards other infectious diseases. Supported by NIH grants GM08247 and A141231.

THE MODULATORY EFFECT OF MUCOSAL ADJUVANTS ON THE EFFICACY OF A RECOMBINANT VEG-BASED CHLAMYDIAL VACCINE, F. Q. Eko (1), E. E. Ekong (1), D. N. Okenu (1), Q. He (1)...

...C. trachomatis proteins. We tested the hypothesis that co-delivery of an rVEG-based chlamydial vaccine with the potent mucosal adjuvant, CT42B will enhance its protective ability. Thus, rVEG vector-based subunit vaccines expressing the chlamydial...

...evaluated in a mouse model of genital infection. Groups of female C57BL/6 mice were immunized by the intramuscular, intravaginal and transcutaneous routes with the vaccine constructs and humoral and

cell-mediated immune responses were evaluated. In addition, the protective efficacy of the vaccine constructs against genital challenge with live Chlamydia was evaluated. Results indicated that co-expression of chlamydial MOMP with CTAB boosted the Chlamydia-specific immune responses irrespective of the route of immunization and conferred a greater degree of protection than the rVOG-MOMP construct. These results indicate that incorporation of mucosal adjuvants in the rVOG delivery platform can enhance the protective immunity of rVOG-based chlamydial vaccines.

EFFECT OF ESTROGEN ON TGASE1 EXPRESSION IN IMMATURE MOUSE VAGINAL... skin development, only preliminary studies have been carried out to investigate TGase1 expression in hormone-response epithelia such as vaginal tissue. Recent experiments in our laboratory have demonstrated that TGase1 is...

...sections of vaginal tissue will then be analyzed for the presence of TGase1 protein by immunohistochemistry utilizing a TGase1 monoclonal antibody. This study may provide valuable insight into the mechanism by...

...Cholerae ghost (rVOG) platform is a suitable delivery vehicle for targeting chlamydial antigens to the immune system leading to significant protective immunity. We hypothesized that the moderate degree of protection obtained in our earlier study may be...

...proteins in the inner membrane of VOG and inadequate presentation of the antigens to the immune system. Since periplasmic targeting of antigens has been shown to be effective in delivering heterologous...

...the maltose-binding protein. Western blot analysis showed a high level of PorB on rVOG. Immunization of mice with rVOG-PorB resulted in the induction of a robust protective Th1 and...

...antibody responses. Significant levels of CD28, CD40L, CD80 and CD86 were also detected in mice immunized with rVOG-PorB. Immunized animals resolved their infection two weeks post-challenge. Thus, targeting PorB to the periplasmic space...

...VOG significantly increased its level of expression and the amount of antigen presented to the immune system leading to an enhanced anti-chlamydial vaccine efficacy.

CHOLESTEROL ACTIVATES THE EXPRESSION OF ANDROGEN-REGULATED PROSTATE-SPECIFIC NON-CODING RNA GENE PCGEM1...

...expression may be of therapeutic importance especially in androgen unresponsive prostate cancer.

ASSOCIATION OF HOST IMMUNOGENETICS AND SEXUALLY TRANSMITTED INFECTIONS ON REPRODUCTIVE HEALTH, Jayanti Mani-Pramanik (1),(3), Shilpa Karkar (1)...

...and Jonathan K. Stiles 1), (1) Morehouse School of Medicine, Department of Microbiology, Biochemistry and Immunology, 720 Westview Drive SW Atlanta, GA 30310, (2) National Institute of Malaria Research (ICMR), Jabalpur...

...of VEGF, VEGFR2 and IL-1Rtl were determined in M1 Lysates by Western blot. Immunohistochemical analyses of angiogenic related antigens: PECAM or CD31 and CD68 in M1 were carried out...

...bearing antigen presenting cells (e.g., dendritic cells, DC) is effective for including a robust immune response against Chlamydia. However, FcR-based vaccine delivery using intact antibody-antigen immune complexes could have pathologic effects in clinical application in humans. We tested the hypothesis that...

...of Fc of IgG and select chlamydial proteins (rFc-OMP) will target DCs



at these mucosal sites for induction of protective immunity against genital Chlamydia infection. Fc-fusion protein of chlamydial MOMP (Fc-MOMP) was generated and used in DC binding studies in vitro, as well as immunogenicity and protection studies in vivo following immunizations. Results revealed that Fc-MOMP was internalized rapidly (within minutes) into pulsed wild-type DC...

...Intranasal or intravaginal administration of Fc-MOMP fusion proteins induced a significantly higher level of mucosal and systemic Th1 response against C. trachomatis serovar D and MoPh (P> 0.002). These results would suggest that these fusion proteins are capable of inducing long-term protective immunity against C. trachomatis.

DIFFERENTIAL EXPRESSION OF KERATINOCYTE TRANSGLUTAMINASE (TGase1) PROTEIN IN RAT REPRODUCTIVE TISSUE IN RESPONSE TO ESTROGEN \*\*, Hillary M. Jarrett \* and W.T. Schroeder, Wesleyan College, Macon, GA 31210. Keratinocyte...

...rats, TGase 1 mRNA expression is induced in vaginal, but not uterine epithelia in response to estrogen. The current project will examine the expression of TGase1 protein in rat uterus...

...1, 3, 6, 12 and 18 hours after administration of exogenous estrogen in ovariectomized rats. Immuno-histochemical analysis will be performed utilizing a mouse anti-human monoclonal anti-TGase1 antibody that...

...and characterized a calcium channel TBCC1 in T. brucei which is a potential drug and vaccine target. We generated a recombinant T. brucei (Ca<sup>sup</sup>.2+) channel peptide antibody (Anti-TBCC1) to assess the expression and localization of the ((Ca<sup>sup</sup>.2+)) channel in the vulnerable flagellar pocket of parasites. The results indicated that TBCC1 is highly immunogenic and formed the basis of our hypothesis that vaccinating against TBCC1 will target (Ca<sup>sup</sup>...

...challenged with T. brucei to assess parasitemia and survival. TBCC1-KLH induced a pro-inflammatory response common to that observed during HAT. This rapid identification and characterization of antigenic targets in ...

...We hypothesize that estrogen promotes Chlamydia infection and its complications by altering the expression of immune modulating cytokines and the production of arachidonic acid metabolites. In this study we used epithelial cells invitro to investigate the effects of estrogen on cytokine expression, prostaglandins production and other immune regulators during Chlamydia infection. The results showed reduced expression of IL-1, IFN-gamma, TNF...

...sections of the vagina will be obtained. The expression of RhoA will be determined through immunohistochemistry and the slides will be analyzed using a Zeiss AxioPlan II research microscope.

EFFECT OF...

...skin development, only preliminary studies have been carried out to investigate TGase1 expression in hormone-response epithelia such as vaginal tissue. Recent experiments in our laboratory have demonstrated that TGase1 is...

...sections of vaginal tissue will then be analyzed for the presence of TGase1 protein by immunohistochemistry utilizing a TGase1 monoclonal antibody. This study may provide valuable insight into the mechanism by...

...of TGase1 is regulated in vaginal epithelium

Posters

DEVELOPMENT OF A BACTERIAL GHOST-BASED DNA VACCINE AGAINST

CHLAMYDIA, Eno E. Ekong (1), Daniel M. Okenu (1), Qing He (1),(2), Joseph

...

...vaccines. Plasmid pVEN-3 encoding major outer membrane polymorphic proteins (OMPs) and FlaB from *Vibrio vulnificus* was constructed by sequentially inserting chlamydial PrpD and omp1 sequences as well as the FlaB...

...confirmed by confocal microscopy and flow cytometry. Further studies will investigate the efficacy of this vaccine in the murine model of *C. trachomatis* genital infection.

KINETICS OF YEAST CATALASE: RETHINKING THE...

30/3, K/44 (Item 2 from file: 149)  
 DI ALCOG R File 149: TGG Health&Wellness DB(SM)  
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02375099 SUPPLIER NUMBER: 103993061 (USE FORMAT 7 OR 9 FOR FULL TEXT)

Nod1 detects a unique muropeptide from gram-negative bacterial peptidoglycan. (Reports).  
 Girardin, Stephen E.; Boneca, Ivo G.; Carneiro, Leticia A. M.; Antignac, Aude; Jehanno, Mugnette; Viala, Jerome; Tedin, Karsten; Taha, Mohamed-Kheir; Labigne, Agnes; Zahringer, Ulrich; Coyle, Anthony J.; Di Stefano, Peter S.; Bertin, John; Sansonetti, Philippe J.; Philpott, Dana J.  
 Science, 300, 5625, 1584(4)

June 6,  
 2003  
 PUBLICATION FORMAT: Magazine/Journal; Refereed ISSN: 0036-8075  
 LANGUAGE: English RECORD TYPE: Fulltext; Abstract TARGET AUDIENCE:  
 Academic  
 WORD COUNT: 2930 LINE COUNT: 00245

TEXT:

Innate immunity to bacterial pathogens relies on the specific sensing of pathogen-associated molecular patterns (PAMPs) by...  
 ... purified *E. coli* LPS (10 (micro)g) or lipid A (10 (micro)g) did not stimulate the Nod1 pathway (Fig. 1A), although they activated macrophages (10). We aimed to identify the...

...have been identified as the major contaminants of LPS preparations responsible for TLR2 signaling after stimulation with commercial *E. coli* LPS (11). We were unable to stimulate the Nod1 pathway by addition of either synthetic lipopeptide or Lpp, the most abundant lipoprotein...

...possible contaminants (fig. S1). Strikingly, we observed that peptidoglycan preparations from Gram-negative bacteria could stimulate the Nod1 pathway, whereas the two Gram-positive peptidoglycan preparations tested here could not (Fig...)

...pivotal role of epithelial cells as the first line of defense against bacterial pathogens at mucosal surfaces. We first prepared extracts from various Gram-negative or Gram-positive bacteria and determined...

...cells do not display an endogenous TLR2/4 sensing system. The only exception was *Salmonella typhimurium* extract; in this case NF-(kappa)B activation is likely to involve TLR5 (21), because extracts from a flagellin-deficient *S. typhimurium* strain were unable to stimulate the NF-(kappa)B pathway (Fig. 3A). A digitonin-based permeabilization technique was then used...

...kappa)B pathway. We observed that extracts from several Gram-negative bacteria were able to stimulate the NF-(kappa)B pathway, whereas

those from the four Gram-positive bacteria were not...

...*S. aureus*, followed by detection of the NF-( $\kappa$ )B p65 subunit nuclear translocation by immuno-fluorescence (Fig. 3B) (fig. S4B). Therefore, these data show that epithelial cells sense Gram-negative...

...that released Gram-positive bacterial peptidoglycan products lack this structure. In the case of *Listeria monocytogenes*, the peptidoglycan contains mesoDAP; however, the peptidoglycan degradation products have not yet been characterized. Of interest, the major peptidoglycan hydrolase in *L. monocytogenes* is a N-acetylmuramoyl-L-alanyl-amidase that cleaves the bond between the peptidoglycan sugar backbone and the peptidic chains. Therefore, *L. monocytogenes* is more likely to release free peptidic chains and amino sugars than substantial amounts of muropeptides (22).

This signaling pathway is independent of MyD88, a key adaptor protein of the TLR/IL-1 pathway (23), because a dominant-negative form of MyD88 was unable to block...

...B pathway induced in digitonin-permeabilized cells by extracts from Gram-negative bacteria, including *S. typhimurium* (DELTA)F, *S. flexneri*, and *E. coli* (fig. S5A) (10). By contrast, using a dominant...

... $\kappa$ B activation induced in digitonin-permeabilized cells by bacterial products from *S. flexneri*, *S. typhimurium*, and *E. coli* (fig. S5B). Several reports have shown that Nod1 activates the NF-( $\kappa$ B)...

...superantigens (Fig. 4) (fig. S7), although tumor necrosis factor  $\alpha$  (TNF( $\alpha$ )) could still efficiently stimulate these cells (Fig. 4). These observations suggest that Nod2 is nonfunctional in epithelial cells in...

...processed by the host cell in the lysosomal compartment, is critical in defining the host response to bacterial infection. In this respect, the characterization of the peptidoglycan motifs sensed by Nod1...

...Nod2 suggests that these two molecules have complementary and nonoverlapping functions that contribute to innate immunity. Moreover, our results show that Nod1 is likely the sole sentinel molecule in the epithelial...

...allowing intracellular detection of bacteria through peptidoglycan sensing, thereby highlighting its key role in innate immune defense.

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...et al., data not shown.

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- (33.) We thank M. Havris for critical reading of the manuscript; the PTR/TLR group at the Institut Pasteur for helpful discussions; those

individuals who donated bacterial strains, plasmids...

...Pathogenie Microbienne Moleculaire, INSERM U389, (2) Unite de Pathogenie Bacterienne des Muqueuses, (3) Groupe d'Immunité Innée et Signalisation, (4) Unite des Neisseria, Institut Pasteur, 28, Rue du Dr. Roux, 75724...

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DESCR PTORS: Immune response--

30/3, K/45 (Item 3 from file: 149)  
 DI ALCO (R) File 149: TGG Health&Wellness DB(SM)  
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01498437 SUPPLIER NUMBER: 16633513 (USE FORMAT 7 OR 9 FOR FULL TEXT)  
 Vaccination against typhoid fever: present status.  
 Ivanoff, B.; Levine, M.M.; Lambert, P.H.  
 Bulletin of the World Health Organization, v72, n6, p957(15)  
 Nov-Dec, 1994  
 PUBLICATION FORMAT: Magazine/Journal ISSN: 0042-9686 LANGUAGE: English  
 RECORD TYPE: Fulltext; Abstract TARGET AUDIENCE: Professional  
 WORD COUNT: 10196 LINE COUNT: 00843

...AUTHOR ABSTRACT: deaths annually in the world. Because of the reactogenicity of the parenteral, killed whole-cell vaccine, research has been oriented towards vaccination orally using live organisms and purified antigen. Live vaccine Ty21a, given by the oral route, has been extensively tested in several studies in developing...

...effective, providing more than 60% protection after 7 years of follow-up. A Vi polysaccharide vaccine has been elaborated and provided more than 65% protection; after 3 years of follow-up...

...the EPI-targeted age groups. The question of whether typhoid fever vaccines interfere with the response to simultaneously administered measles vaccine must also be studied. New live vaccines, given by the oral route in one dose...

...These strains could be used as live vector to deliver foreign antigens to the intestinal mucosa.

... and Smith in the USA recognized the spread of the disease by contagion and the immunity conferred by illness. In 1873 Budd[2] in Engl and provided evidence that bowel discharges were...

...In 1896, Pfeiffer & Kolle[33] in Germany and Wight[49] in England prepared the first vaccine for human use with heat-killed organisms, and demonstrated that antibodies could passively protect guinea... ingestion, the typhoid organisms pass through the pylorus to the small intestine, rapidly penetrating the mucosal epithelium to reach the lamina propria where an influx of macrophages ingest the bacilli but...

...by Kauffman & White. Its antigenic formula, established on the basis of its somatic (O) and flagellar (H) antigens, is [O9, 12, (Vi), d]. It is motile, with a peritrichous flagella (H - d antigen), which is also encountered in approximately 80 other biotypes of Salmonella Strains...

... Vi antigen (thermolabile), which is also present in *Q*itrobacter, *S.* dublin and *S.* paratyphi C.

#### Immunology

The circulating, secretory and cell-mediated immune response is stronger overall after natural infection than after vaccination[27, 29] and includes both prominent serum and cell-mediated components. Parenteral, killed whole-cell (WC) vaccines elicit a serum response equal to a natural infection, but not a comparable cell-mediated response. With the live oral vaccines the opposite is true. Described below are the immune responses after vaccination and the so-called "herd immunity".

#### Immune response after vaccination

Because of the complex nature of the pathogenesis of *S. typhi* clinical infection, a protective role is probably played:

- by the secretory intestinal antibody in preventing mucosal invasion;
- by the circulating antibody against bacteraemic organisms; and
- by cell-mediated immunity in eliminating intracellular bacilli.

The immune response depends on the nature of the vaccine. With parenteral vaccines the circulating antibody response is substantial and presumably provides the predominant protective effect. In contrast, with live oral vaccines the circulating antibody response is modest, but a vigorous cell-mediated immune response occurs, increasing the protection conferred by the vaccine.

With parenteral whole-cell vaccine, elicitation of serum H antibodies and sometime Vi antibodies[47] correlates with protection, whereas O antibodies do not. In contrast, with live oral vaccines, the cell-mediated immune response seems to be directed towards the O and H antigen and not towards the Vi...

...the O antibodies are IgM (LPS (lipopolysaccharide antigen) is T independent), while the H antibody response is initially IgM and then becomes IgG. With purified Vi polysaccharide vaccine the response depends on the preparation of the antigen[41]. Oral, killed WC vaccine stimulates meagre serum O, H, or Vi antibody responses. Attenuated strains elicit relatively weak serum antibody...

...that are intermediate between those after parenteral killed and oral killed vaccines.

The serum antibody response has been most extensively studied with vaccine strain Ty21a. Furer and Germanier[11] noted that Ty21a grown in the presence of galactose, which leads to bacilli bearing smooth LPS, was highly protective, whereas vaccine grown in the absence of galactose, which leads to rough bacilli, was not. He noted a significantly greater seroconversion of O antibody in recipients of vaccine grown in the presence of galactose. Serum levels of IgG and IgA antibodies to S...

...vaccination of healthy Chileans who received Ty21a in one of two formulations, and in various immunization schedules (enteric-coated and gelatin + NAHCQ Sub.3] vaccines). An ELISA method showed, among...

...enteric-coated capsules, a strong correlation between the seroconversion rate of IgG O antibody and vaccine efficacy in the field. Thus, while serum O antibody is not believed to be the operative mechanism of immunity elicited by attenuated strains, it clearly correlates, in this case, with protection.

Secretory antibody response. The intestinal secretory antibody response of any of the vaccines (parenteral, killed oral, live oral) has not been studied in...

...of recipients. However, several studies have shown that local antibody (IgAs) to O antigen was stimulated following oral vaccination with

live oral vaccines, particularly in individuals from endemic areas.

Mucosal tissues contain their own local immune system working in separation from the generalized immune system[14], but activated lymphocytes from the gut can disseminate immunity to other mucosal and glandular tissues. An important basis for local immunity is the migration of specific, antigen-activated B and T cells from Peyer's patches...determinants - so-called addressins, which are specific for lymphocyte homing receptors on endothelial cells - in mucosal and glandular tissues, they will return to and extravasate into these tissues. Most of the...

...cells move to the intestinal epithelium but a substantial proportion (10-25%) end up in mucosal tissues outside the intestine.

B cells in the lamina propria synthesize the IgA molecules as...

...with a small piece of SC remaining in the membrane.

Kantel[17] studied the human immune response (in persons vaccinated 2 years previously by oral Ty21a vaccine) to a secondary immunization by the same oral vaccine by enumerating the specific antibody-secreting cells (ASC) in the peripheral blood. This study shows the presence of immunologic memory in respect of the human ASC response, and confirms the separate nature of ASC and serum responses. Serum antibody responses were not seen in any of the vaccinees after secondary immunization, whereas after primary immunization 60% of these subjects responded.

T-cell response. Cell-mediated responses have been measured, following vaccination with parenteral, killed, VC vaccines or live...

...soluble antigen, or inhibition of growth of S. typhi by mononuclear cells. Live oral vaccines stimulate the more potent T-cell immune response[40], which appears to be largely directed against the O antigen. Following oral immunization with S. typhi Ty21a[39], or 0901[27], or 541 Ty[24], the appearance of...

...S. typhi has been observed. Preliminary evidence showed that the necessary component in plasma is immunoglobulin and that IgA is most effective.

Herd immunity

An indirect protective effect has been observed in control groups during field trial studies of...

...on what might possibly occur following a systematic wide-scale application of Ty21a live oral vaccine in TF control programmes[21].

The incidence rate in the randomized control group in the...

...000 children in Areas Sur and Central were given 2, 3 or 4 doses of vaccine. In this third year of surveillance the incidence in the placebo group fell again by...

...additional Santiago children were entered into a trial, 88% of whom received three doses of vaccine, the others receiving placebo. Approximately 80% of these children were in Area Sur Oriente, the rest were young children in Area Norte who entered school after initiation of the 1982 vaccine trial in Area Norte. During this fifth year of surveillance, the incidence of TF in...

...administration and their composition.

Vaccines given by parenteral and aerosol routes

Killed organisms or subunit immunizing antigens have been used.

(1) Vaccines composed of killed organisms

Parental, killed VC vaccine inactivated by heat, phenol, or acetone has been used since 1896. Between 1960 and 1970...

... trials. The first, held in Yugoslavia showed that a fluid, heat-inactivated, phenol-preserved parenteral vaccine was superior in protective efficacy when compared with an alcohol-inactivated and preserved vaccine. After this trial the Walter Reed Army Institute of Research prepared for WHO two lyophilized vaccines for use in other field trials[45]. These included a heat phenol-inactivated vaccine (L) and an acetone-inactivated vaccine (K) tested in randomized, controlled, double-blind trials in Yugoslavia[50] and Guyana. In addition, the K vaccine was evaluated for efficacy in Poland and the L in Russia.

Results are presented in Table 2. The K vaccine was found to provide significantly more protection than the L vaccine.

[TABULAR DATA OMITTED]

Although protective, killed WC vaccines are rarely used in systematic TF control...

... attempts have been made to prepare extracts and sonicates of *S. typhi*. The various subunit immunizing agents, which were called "chemical" vaccines include the following:

- freeze and thaw extract vaccines; - trypsinized...

... Robbins et al. [34] utilized a non-denaturing technique of extraction to prepare an effective vaccine.

Some chemical vaccines have been used by either the parenteral or aerosol route.

(3) Vaccine composed of Vi polysaccharide

History. The Vi polysaccharide of *S. typhi* is a homopolymer of... covers the bacteria as a capsular antigen and correlates with its virulence. A poor serological response to Vi antigen has been shown in acute TF which contrasts with the very high response in most chronic carriers. Vi protected the O antigen of *S. typhi* from agglutination by...

... it in a very highly purified form. But the technique employed was denaturing and the vaccine failed to protect volunteers. Vong[48] purified the Vi polysaccharide by a non-denaturing technique with hexadecyl trimethyl ammonium bromide, which he used as a parenteral vaccine. More recently this work was extended by Robbins who prepared with Merieux the "Thyphim Vi" vaccine.

Safety and immunogenicity studies with purified Vi antigen. Tacket[41] evaluated immunogenicity of two nondenatured Vi lots prepared at NIH Bethesda (USA) or at the Merieux Institute...

... titres of Vi antibody in about 90% of recipients. However, the less pure lot also stimulated O antibody in more than 80% of vaccinees. In contrast, the 99.8% pure preparation was well tolerated and stimulated O antibody in fewer than 20% of vaccinees. Moreover, Tacket[42] showed that the Vi antibodies generated in the vaccinees persisted at least three years.

Field trials with purified Vi vaccine. Two randomized controlled field trials were initiated in Nepal[1] and in South Africa[18] to assess the safety and efficacy of the candidate Vi vaccine produced by the Merieux Institute. Control groups received anti-meningococcal vaccine in South Africa and anti-pneumococcal vaccine in Nepal. In both trials the vaccine was well tolerated. In Nepal[1], a single 25mg intramuscular dose provided 72% protection for...

... a combination of active and passive surveillance methods.

Table 3. Culture-confirmed TF in persons immunized with Vi or control (pneumo or meningo) polysaccharide antigens

Site and	No. of	No. of	Incidence/	Efficacy
Page 103				

vaccine	vaccinees	typhoid cases	[10. sup. 5] / yr	(%)
Nepal:				
Vi	3457	9	260	72
Pneumo	3450...			

... results of these two trials, where surveillance is being continued to determine the duration of immunity, clearly establish the efficacy of typhoid vaccines based on humoral immunity to the Vi antigen.

A safety and immunogenicity study has been conducted in 158 children aged 2 to 10 years old. The first...

... S. typhi can be exhibited in the absence of Vi antibody, since the protective oral vaccine Ty21a lacks Vi antigen and therefore does not stimulate Vi antibody. This raises the question of whether maximal protection against TF might be obtained by combining a vaccine that stimulates Vi immunity with a live oral vaccine, such as Ty21a, which elicits humoral and cell-mediated immunity against non-V antigens [21].

Vi vaccine is currently licensed by Merieux Institute ("Thyphim Vi") in Chile, Congo, Cote d'Ivoire, France...

... Togo and the United Kingdom

Vi polysaccharide conjugate vaccines. In an attempt to increase the immunogenicity of Vi as a parenteral vaccine, Szu et al. [37, 38] conjugated Vi polysaccharide to tetanus toxoid, diphtheria toxoid and cholera toxin, conferring T-dependent properties on the polysaccharide. The candidate conjugate vaccine elicited higher levels of serum antibodies than purified Vi alone in two animal species, mice and rhesus monkeys. Immunized animals responded to a booster dose with conjugate vaccine, by exhibiting further increases in Vi antibody titre. In contrast, booster doses of purified Vi polysaccharide failed to increase the level of Vi antibody.

Potential characteristics of the Vi conjugate vaccine are: - they are more immunogenic in young animals, but require multiple doses to achieve maximal antibody titres; - they will most... absence of streptomycin. It was shown to be safe and effective as a live oral vaccine in studies on volunteers. However, in subsequent studies, protection was not conferred when the vaccine was administered with reconstituted lyophilized organisms. Although these studies were abandoned, experience with the streptomycin...

... in the absence of galactose, Ty21a does not express smooth O antigen and is not immunogenic. In the absence of UDP galactose-4-epimerase, the galactose residues can be obtained through...

... bacterial death by lysis, which has been presumed to account for the failure to recover vaccine organisms from coprocultures of persons who ingested the usual dose of 1 to 5 x [10. sup. 9] organisms.

In preliminary safety and immunogenicity studies in adult North Americans, Ty21a (grown in a low concentration of galactose) was well tolerated, even with oral doses as high as [10. sup. 11] organisms and was immunogenic [23].

Field trial in Egypt

The first field trial of efficacy was conducted from 1978...

... 6 to 7 years were randomized to receive three doses ([10. sup. 9] organisms) of vaccine or placebo administered every other day. Each dose of lyophilized vaccine was reconstituted in the field with a diluent to create a liquid suspension and was...

... case in the vaccinated group (96% efficacy).

After these encouraging results the Swiss Serum and Vaccine



Institute in 1981 prepared a commercial formulation of Ty21a in gelatin capsules containing a dose of lyophilized vaccine together with two additional gelatin capsules, each containing 0.4 g of NaHCO<sub>3</sub> Q sub...

...of the commercial formulation (gelatin capsules containing NaHCO<sub>3</sub> Q sub.3]) compared with the lyophilized vaccine which was marketed after the Egyptian trial? - Could a longer interval between the doses enhance the immunogenicity of the vaccine? - Could an immunological assay be identified that would correlate with levels of vaccine efficacy in a field trial, which could be used to predict the effect of changes in formulation and immunization schedules?

Many of these points were successfully investigated in a series of four field trials of vaccine efficacy carried out in Chile with Ty21a vaccine[22].

Three of the four studies were conducted with placebo groups. The first two field...

...was isolated from blood, bone marrow, or bile-stained duodenal fluid) were used in reckoning vaccine efficacy.

Area Occidente (western) field trial 1983-86). More than 140 000 children were randomized to one of five groups that received vaccine or placebo as follows:

- Group 1: three doses of vaccine in enteric-coated capsules with two days' interval.
- Group 2: three doses of vaccine with NaHCO<sub>3</sub> Q sub.3], - gelatin formulation, with two days' interval.
- Group 3: three doses of vaccine in enteric-coated capsules, with an interval of 21 days between the doses.
- Group 4: three doses of vaccine with NaHCO<sub>3</sub> Q sub.3], gelatin formulation, with an interval of 21 days between the doses.
- Group 5: three doses of placebo with 2 days' interval.

The vaccine contained 1 to 3 x [10.sup.9] viable organisms per dose. Since TF exhibits...

...over administering all three doses within a week; and - the level of protection (over 60% vaccine efficacy) conferred by the best regimen, given two days apart, persisted for at least seven...

...356 school children were randomized in three groups as follows:

- Group 1: two doses of Ty21a vaccine in enteric-coated capsules (1 to 3 x [10.sup.9] organisms per dose).
- Group 2: one dose of vaccine and 1 dose of placebo identical in appearance.
- Group 3: two doses of placebo.

The doses of vaccine were given to the children 1 week apart.

The main points are as follows: - two doses of enteric-coated vaccine provided protection (52% to 71% for a period of two years, which then dropped to...

...year and was nonexistent in the fourth year of surveillance; and - a single dose of vaccine in enteric-coated capsules provided low levels of protection for two years, which dropped in...

...the feasibility of using Ty21a as a public health tool in large-scale school-based immunization programmes, and also to determine if administration of four doses of vaccine within an 8-day vaccination period could enhance protection. Some 190 000 children were randomized to receive two, three or four doses of Ty21a vaccine in enteric-coated capsules (1 to 3 x [10.sup.9] organisms per dose), within...

...years of surveillance show that the incidence of TF in recipients of three doses of vaccine was only slightly lower than that in children who received two doses. In contrast, the...

...efficacy recorded in Alexandria. The following explanations can be proposed:

(1) Human genetic differences. The immune response to *Haemophilus influenzae* type b purified polysaccharide exhibits genetic restriction. It is possible that the Egyptian children mount better immune responses to Ty21a than Chilean children, based on genetic differences[13]. (2) Antigenic differences in...

...a lyophilate, whereas in Santiago the children ingested lyophilized organisms contained within enteric-coated capsules. Vaccine organisms may be more viable when reconstituted in vitro before feeding than if they must...

...are exposed to bile acids, enzymes, and degraded food. Moreover a liquid suspension allowed the vaccine organisms to be in contact with the tonsils, a lymphoid organ.

[TABULAR DATA OMITTED]

Field...1206 per 100 000 per year. One explanation for the lower protective efficacy of the vaccine in Indonesia than in Chile is that immunity was overcome by more frequent inoculations of greater numbers of bacteria with intense transmission of...

...against infection with *S. paratyphi A*. In the Santiago field trial, one dose of Ty21a vaccine resulted in 22% efficacy against *S. paratyphi B* and two doses resulted in 54% efficacy...

...safe and efficacious, it suffers from some drawbacks, including the requirement for multiple doses to stimulate protection, the fragility of the vaccine strain in the fermentation and lyophilization processes of large-scale manufacture, and the fact that...

...of *S. typhi* that might serve as oral vaccines. It is hoped to obtain successful immunization with just a single oral dose.

Mutation affecting regulatory pathways  
Investigators at Washington University, Ied...

...in strain X4073. The latter mutation was intended to diminish or prevent invasion of the vaccine strain beyond the intestinal lymphoid tissue to deeper organs of the reticuloendothelial system. When fed to volunteers at dosages of [10.sup.5] and [10.sup.6] organisms, this vaccine was found to be non-reactogenic and to induce serum anti-o antibodies and antibody...

...H antigens that were somewhat better than those seen after administration of Ty21a. Moreover, the vaccine organism could not be recovered in blood cultures. However, febrile adverse reactions (accompanied by bacteraemia) and loose stools were observed in some individuals who received this vaccine strain used as a live vector carrying a plasmid encoding a hepatitis B virus antigen.

Miller[28] from Boston constructed a mutant strain PhoP. It is a derivative of *S. typhimurium* with mutation on the virulence regulon which is composed of the PhoP (transcriptional regulator) and...

...Three regulated loci (pagC, pagD and prgH), when singly mutated, affect the virulence of *S. typhimurium* for mice. The *phoP*, *phoQ*, *pagC* and *pagD* genes are highly conserved between *S. typhimurium* and *S. typhi*.

Mutation affecting biosynthetic pathways

Another approach involves mutations in genes affecting biosynthetic

...mammalian tissues.

This approach was chosen by Levine and coworkers[23] at the Center for Vaccine Development in Baltimore to construct strain 541Ty (Aro-, pur-, Vi-) and a Vi-negative variant strain 543Ty (Aro-, pur-, Vi-). In a clinical evaluation for safety and immunogenicity, these two strains caused no adverse reactions in 37 adult American volunteers who ingested

doses as high as  $10 \times 10^9$  vaccine organisms with buffer. A good cellular immune response was obtained [24]. However, only meager humoral responses were induced in a small percentage of...

...a single biosynthetic pathway.

Levine, Hone and co-workers then created an attenuated *S. typhi* vaccine candidate, CVD 906 [15], by introducing precise deletion mutations in two genes *aroC* and *aroD*...

...one dose of  $5 \times 10^8$  CFU it elicited a good humoral and mucosal immune response in 80% of U.S. volunteers; no Vi antibodies have been recovered in sera and 2 out of 9 volunteers got diarrhoea. Because of its reactogenicity, another candidate vaccine, CVD 908, has been constructed on a similar model from a less invasive strain [ $4.5 \times 10^8$  to  $5 \times 10^8$ ] organisms and a good response in IgA anti-LPS antibody-secreting cells. However, systematic daily culturing of blood from vaccinees during the first 12 days following ingestion of CVD 908 vaccine resulted in isolation of the vaccine strain from the majority of volunteers (50% at 101 to 100% at  $10^8$ ...

...live vector expressing foreign antigens of *Plasmodium falciparum* or of pathogenic bacteria.

As CVD 908 vaccine enters phase II clinical trials to assess its safety and immunogenicity in larger numbers of subjects, attention will be paid to determine if there is any clinical significance associated with the isolation of vaccine organisms from blood cultures during the 4-10 days after vaccination. Further studies are planned...

...before deciding to vaccinate a large number of people. Which groups should be vaccinated? Which immunization schedules should be used? What is the conservation time of the vaccine and the duration of protection? What kind of recommendations should be given?

Groups to be...

...Vi polysaccharide are already licensed in many countries. Little is known about the safety and immunogenicity of both these vaccines in infants. Murphy [30], in a preliminary study in Chile, has...

...toddlers, particularly those aged 6 to 24 months, and elicits a much smaller serum antibody response compared with that in older children. However, Murphy used a particular formulation of Ty21a, i...

...water (dilution in milk was impossible). Oanratane [32] and Cryz [4] studied the safety and immunogenicity of Ty21a in a liquid formulation in Thai children aged 4 to 6 years of age. The immune response to Vi vaccine is currently being studied in children aged 6 months to 4 years, the first results showing a good immune response in all children during the first 3 months of follow-up, with a slight decrease...

...children who account for the highest incidence of TF and are amenable to school-based immunization programmes; both vaccines are protective in this age group. However, in some countries this age...

...Ty21a must be kept refrigerated and requires a cold chain; freezing will not harm the vaccine. In contrast, the Vi PS vaccine is not adversely affected by elevated temperatures in tropical areas and probably requires no cold chain.

Immunization schedules. Oral vaccine Ty21a: three oral doses of Ty21a in enteric-coated capsules are given on day 1...

...level of protection can be increased by administration of a fourth dose of enteric-coated vaccine or by using a liquid formulation on day 7. The oral route is usually well accepted and facilitates mass administration by non-professionals. Parenteral Vi vaccine: A single parenteral inoculation with purified Vi vaccine gave similar levels of protection for at least 2-3 years after vaccination (efficacy, 65...

...large follow-up report has been published on the level of protection of the Vi vaccine; however, a good anti-Vi antibody level was recovered three years after vaccination[42].

Recommendations...

...Clerens, J. Holmgren, M.M. Levine and J. Mekalanos) from the WHO/UNDP Programme for Vaccine Development evaluated the currently available anti-typhoid vaccines, defined their use in public health, and made the following recommendations:

(1) The reactogenicity of the current heat-phenol killed typhoid vaccine negates its usefulness as a public health tool. Countries wishing to incorporate vaccination against typhoid...

...overwhelmingly supports use of the liquid formulation rather than enteric-coated capsules of the Ty21a vaccine. (2) For routine vaccination programmes, school-based vaccination may be appropriate in some areas; where...

...be preferred. Unfortunately, the latter strategy cannot be pursued until a suitable, safe and protective vaccine is found for administration to the EPI-targeted age groups. (3) The decision to incorporate vaccination against typhoid into a country's immunization programme should ideally be based on careful consideration of the local epidemiology of typhoid, including...

...high risk, as well as quantitative analysis of the costs and benefits of the typhoid vaccine to be included. (4) Further research, supported by WHO, is required for both Ty21a and Vi vaccines on the following issues:

(a) More information is required about the immunogenicity and safety of these vaccines when administered to infants at the age scheduled for measles vaccine (9 or 12 months in most typhoid-endemic areas). Such studies should not only evaluate immune responses to each vaccine at this age, when compared with administration at an older age (e.g. 24 months), but also assess whether the typhoid vaccine interferes with responses to simultaneously administered measles vaccine.

(b) If studies outlined in (a) yield encouraging results, the efficacy of the typhoid vaccines, co-administered with measles vaccine, should be formally evaluated in a population with endemic typhoid.

(c) Because the duration of protection conferred by Vi vaccine is uncertain, information about this parameter is needed from field trials conducted in all age...

...the intensity of S. typhi infections, may modify the level of protection for any given vaccine, the efficacy of Ty21a and Vi vaccines from different field trials should be compared when...

...to the same population.

(e) Because Ty21a and Vi vaccines appear to protect via different immunological mechanisms and because each vaccine confers only moderate protection, it is of great interest to assess whether combined administration of...

...undertaken with a formal field trial.

(f) For countries deciding to incorporate Ty21a or Vi vaccine in public health control programmes, phase-4 evaluations of safety and

efficacy, using observational designs...

...should be encouraged to work with typhoid endemic countries to enable local production of the vaccine with suitable quality control procedures.

#### Conclusion

Because of the reactogenicity of the parenteral, killed whole-cell typhoid vaccine, research was directed towards oral vaccination using live organisms, which have been effective in public health programmes. The widespread application of Ty21a, one such oral vaccine, can result in a "herd immunity" effect.

Some new vaccine strains prepared by genetic engineering could improve the currently obtained results. For example, it would be interesting to get an immunizing regimen that could elicit Vi antibody besides the non-Vi humoral and cellular immune response stimulated by an attenuated *S. typhi*. A Vi positive mutant of Ty21a[3, 43], when given by...

...*S. typhi* (26% of them developing Vi seroconversion). However, protective efficacy (provided either by Ty21a vaccine or by Vi vaccine) suggests combined immunization using oral Ty21a and parenteral purified Vi.

#### Resume

La vaccination antityphoïdique: situation

La fièvre typhoïde...

...en sante publique. Cependant, avant d'etre utilisees dans ce but, leur innocuite et leur immunogenicite devront etre evaluees a l'age auquel les vaccins du PEV sont donnees. De plus...

...faudra egalement verifier que l'administration du vaccin antityphoïdique n'interfere pas avec la reponse immunitaire stimulee par le vaccin antirougeoleux.

De nouveaux vaccins vivants administrables par voie orale ont ete mis

...

...vivants pour produire des antigenes au niveau de la muqueuse intestinale, entrainant ainsi une reponse immunitaire de cette muqueuse.

(1) WHO Global Programme for Vaccines and Immunization, Vaccine Research and Development, World Health Organization, 1211 Geneva 27, Switzerland. Requests for reprints should be sent to this address. (2) Center for Vaccine Development, University of Maryland, School for Medicine, Baltimore, MD, USA.

(a) Ty21a vaccine is licensed by Berna and other laboratories ("Vi votif") and by Sclavo ("Neotif") in 28 countries...

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TLR Polymorphisms and the Risk of Invasive Fungal Infections  
(Editorial)

Pamer, Eric G.  
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TLR Polymorphisms and the Risk of Invasive Fungal Infections  
(Editorial)

#### TEXT

...cell transplantation is a potentially lifesaving cancer therapy that, at least temporarily, renders patients highly immunocompromised and vulnerable to infection. Aspergillus fumigatus, a common environmental fungus that causes invasive infections in immunocompromised persons, is particularly problematic in patients who have undergone this treatment. (Ref. 1) Although the risk of the development of aspergillosis correlates with the degree of immunosuppression and the intensity of exposure to fungal spores, these factors alone do not explain why...

...the Journal (Ref. 2) begins to shed light on additional risk factors by correlating innate immune-receptor polymorphisms with the risk of the development of invasive aspergillosis after allogeneic hematopoietic stem ...

...Innate immune receptors are expressed on or within mammalian cells and, on binding to microbial molecules, induce...

...restrict microbial tissue invasion and enhance microbial killing. (Ref. 3) The most extensively investigated innate immune receptors are the toll-like receptors (TLRs). Toll, a protein first described in Drosophila melanogaster...

...a regulator of development in flies, (Ref. 4) was subsequently discovered to mediate an innate immune defense against fungal infection in fruit flies by inducing production of the antimicrobial peptide drosomycin. (Ref. 5) A long hunt for innate immune receptors

in mammals led to the discovery of TLR4, (Ref. 6,7) the receptor that...  
...with distinct specificities that extend from microbial glycolipids and  
lipoproteins to nucleic acids and bacterial flagellins. (Ref. 3)...

...Studies in mice show increased susceptibility to infection when  
TLR signaling is impaired, and mutations in genes encoding TLRs or  
downstream signaling proteins increase the...

...a common mutation resulting in a deficiency of TLR5, a receptor that  
responds to bacterial flagellin, is associated with increased  
susceptibility to *Legionella pneumophila* infection. (Ref. 9) Point  
mutations in TLR2...

...Single-nucleotide polymorphisms (SNPs) in four TLR genes (TLR2,  
TLR3, TLR4, and TLR9) were characterized in transplant recipients and  
donors; one haplotype...

...with invasive aspergillosis was significant only in recipients of  
unrelated allografts, who presumably required greater  
immunosuppressive therapy to prevent graft-versus-host disease; this  
suggests that the "susceptibility phenotype" may be apparent only in  
patients with more profound degrees of general immunosuppression.  
Furthermore, the S4 haplotype of the donor, but not the recipient, was  
associated with invasive aspergillosis, indicating that TLR function  
in bone marrow-derived cells -- perhaps in neutrophils, monocytes,  
macrophages, or dendritic cells -- is...

...*A. fumigatus* infection might be considered surprising, since this  
receptor is involved principally in the response to bacterial  
lipopolysaccharides. Since *A. fumigatus* does not produce  
lipopolysaccharides, TLR4 may bind other, nonlipopolysaccharide...

...TLR-mediated activation of innate immune effector cells  
(e.g., macrophages, granulocytes, or dendritic cells) provides a direct  
mechanism to inactivate pathogenic microbes. (Ref. 3) An alternative  
indirect mechanism for a TLR-mediated defense against invasive  
infections has been suggested by recent studies of innate immune  
responses to microbial colonization of mucosal surfaces. Commensal  
bacteria inhabiting the intestine, for example, stimulate TLRs,  
including TLR4, and induce the expression of antimicrobial molecules by  
epithelial cells. (Ref. 13,14) Thus, even in the absence of overt  
infection, the innate immune system in mammals actively responds to  
colonizing bacteria and establishes an "innate immune tone" that  
fortifies mucosal barriers and restricts microbial invasion...

...Can differences in the sensitivity of TLRs for their respective ligands  
affect the innate immune tone? Circulating levels of acute-phase  
reactants in persons expressing TLR4 variants suggest that the basal innate  
immune tone correlates with TLR sensitivity to  
lipopolysaccharides. (Ref. 15) So, an alternative explanation for the  
finding of Bochar et al...

...persons receiving stem cells that express the high-affinity TLR4 variant  
have an elevated innate immune tone that, more generally, increases  
resistance to infection. Determining how TLR polymorphisms influence  
a defense against pathogens will make for an exciting scientific journey  
that may

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30/3, K/47 (Item 2 from file: 444)  
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Medical Progress: Typhoid Fever (Review Article)

Parry, Christopher M; Hien, Tran Tinh; Dougan, Gordon; White,  
Nicholas J.; Farrar, Jeremy J.  
The New England Journal of Medicine  
Nov 28, 2002; 347 (22), pp 1770-1782  
LINE COUNT: 00651 WORD COUNT: 08992

# TEXT

...the family Enterobacteriaceae. The bacterium is serologically positive  
for lipopolysaccharide antigens O9 and O12, protein flagellar antigen  
Hd, and polysaccharide capsular antigen Vi. The Vi capsular antigen is  
largely restricted to...

...strains of S. enterica serotypes hirschfeldii (paratyphi O) and dublin,  
and Citrobacter freundii. A unique flagella type, H<sub>1</sub>, is present in  
some S. enterica serotype typhi isolates from Indonesia. (Ref. 13)...  
...estimated 4599 coding sequences. The genomes of S. enterica serotype  
typhi CT18, S. enterica serotype typhimurium LT2, (Ref. 18) and  
Escherichia coli (Ref. 19) are essentially collinear, despite the fact that  
...amounts of antacids lowers the infective dose. In the small intestine,  
the bacteria adhere to mucosal cells and then invade the mucosa  
...The M cells, specialized epithelial cells overlying Peyer's patches, are  
probably the site of...

...point that is probably determined by the number of bacteria, their  
virulence, and the host response, bacteria are released from this  
sequestered intracellular habitat into the bloodstream. The incubation  
period is...

...Typhoid induces systemic and local humoral and cellular immune  
responses, but these confer incomplete protection against relapse and  
reinfection. The interaction of host immunologic mediators and

bacterial factors in infected tissue may contribute to the necrosis of Peyer's...

...disease. (Ref. 30) The evidence for an association between typhoid and infection with the human immunodeficiency virus (HIV) is conflicting, (Ref. 31,32) whereas there is a large increase in the...times that for fully susceptible strains. This reduction in susceptibility results in a poor clinical response to treatment. (Ref. 48,49) Quinolone resistance is frequently mediated by single point mutations in...

...although there are sporadic reports of fully fluoroquinolone-resistant isolates. (Ref. 51) Because the clinical response to fluoroquinolones in patients infected with nalidixic acid-resistant strains is greatly inferior to the response in those infected with nalidixic acid-susceptible strains, we believe that the break points for... cross-reacting epitopes with other Enterobacteriaceae. Furthermore, patients with typhoid may mount no detectable antibody response or have no demonstrable rise in antibody titer. Despite this, some centers have found Widal...provision of safe drinking water, effective sewage disposal, and hygienic food preparation. (Ref. 4) Mass immunization has been used successfully in some areas. (Ref. 94) In developed countries, identification of chronic...

...The first parenteral whole-cell typhoid vaccine was introduced in 1896. Its efficacy was established in field trials in the 1960s in...

...young adults, lasting for up to 12 years. The chief disadvantages of the whole-cell vaccine are local discomfort and swelling and the systemic side effects that occur in 25 to...

...Field studies of Ty21a, a live, attenuated oral vaccine, have shown variable protective efficacy, ranging from 96 percent after 3 years in Egypt (Ref. ...

...53 percent, depending on the formulation, after 2.5 years in Indonesia. (Ref. 98) The vaccine is given as one capsule on days 1, 3, 5, and 7 and is suitable...

...children over six years of age. A booster dose is recommended every five years. The vaccine is well tolerated, but because it is a live, attenuated vaccine, it should not be given to immunocompromised patients or ...The parenteral Vi-based vaccine is suitable for adults and children over the age of two years and has no...

...administered intramuscularly. Booster doses are recommended every two years. A single injection of the Vi vaccine provided a protective efficacy of 72 percent after 17 months in Nepal (Ref. 99) and 64 percent after 21 months in South Africa. (Ref. 100) A new modified Vi vaccine conjugated to a nontoxic recombinant *Pseudomonas aeruginosa* exotoxin A (rEPA) was evaluated recently in Vietnam...

...year, the protective efficacy was 91.5 percent. (Ref. 101) An important advantage of this vaccine is that it has the potential to be immunogenic in infants under the age of two. There is no currently licensed vaccine against *S. enterica* serotype paratyphi A...

...are effective outside areas of endemic disease. In areas where epidemic risk is high, mass immunization should be considered during disasters or in refugee camps, in combination with adequate provision of...

...reduced dramatically by a program of yearly vaccination of school children with the old whole-cell vaccine. (Ref. 94) The emergence of antimicrobial resistance may change the balance of cost effectiveness for...

... A typhoid-vaccination program for school children or, with the advent of the new conjugate Vi vaccine, as part of the Expanded Program of Immunization, should be considered...

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